Clinical Policy: Desmopressin Acetate (DDAVP, Stimate, Nocdurna, Noctiva)
Reference Number: CP.PHAR.214
Effective Date: 05.01.16
Last Review Date: 02.20
Line of Business: Commercial, HIM*, Medicaid

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

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

*For Health Insurance Marketplace (HIM), Nocdurna and Noctiva are non-formulary and should not 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.

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.

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, Nocdurna, 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 ≥ 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 ≥ 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:
   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 ≥ 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:
Medicaid/HIM – 6 months
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 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
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. 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:
Medicaid/HIM – 12 months
Commercial – DDAVP injection: 6 months or to member’s renewal date, whichever is longer; Stimate/Nocdurna/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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>desmopressin acetate oral tablets (DDAVP®)</td>
<td>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</td>
<td>1.2 mg/day</td>
</tr>
</tbody>
</table>

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):
     o DDAVP injection: moderate to severe renal impairment (creatinine clearance < 50 mL/min), hyponatremia or a history of hyponatremia
     o Stimate: none reported
     o 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 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
     o 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 m²; syndrome of inappropriate antidiuretic hormone (SIADH) secretion, during illnesses that can cause fluid or electrolyte imbalance, heart failure; uncontrolled hypertension
   • Boxed warning(s):
     o DDAVP injection, Stimate: none reported
     o 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.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desmopressin injection (DDAVP)</td>
<td>Central diabetes</td>
<td>2 to 4 mcg IV or SC daily, usually</td>
<td>4 mcg/day</td>
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<td></td>
<td>insipidus</td>
<td>in 2 divided doses</td>
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<tr>
<td></td>
<td>Hemophilia A, VWD</td>
<td>0.3 mcg/kg IV or SC as needed</td>
<td>0.3 mcg/kg/dose</td>
</tr>
<tr>
<td>Desmopressin nasal spray (Stimate)</td>
<td>Hemophilia A, VWD</td>
<td>One spray per nostril</td>
<td>300 mcg/dose</td>
</tr>
<tr>
<td>Desmopressin sublingual tablet</td>
<td>Nocturnal polyuria</td>
<td>Women: 27.7 mcg PO QD one hour before</td>
<td>Women: 27.7 mcg/day; Men: 55.3 mcg/day</td>
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<tr>
<td>(Nocdurna)</td>
<td></td>
<td>bedtime</td>
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<td></td>
<td></td>
<td>Men: 55.3 mcg PO QD one hour before</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>bedtime</td>
<td></td>
</tr>
<tr>
<td>Desmopressin nasal spray (Noctiva)</td>
<td>Nocturnal polyuria</td>
<td>One spray in either nostril</td>
<td>1.66 mcg/day</td>
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<td></td>
<td></td>
<td>approximately 30 minutes before</td>
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<td></td>
<td></td>
<td>bedtime; dose varies by age and</td>
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<td></td>
<td></td>
<td>hyponatremia risk:</td>
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<td></td>
<td>- Patients &lt; 65 years without</td>
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<td></td>
<td>increased risk for hyponatremia: 1.66 mcg/spray</td>
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<td></td>
<td></td>
<td>- Patients ≥ 65 years or younger</td>
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<td>patients at risk for hyponatremia: 0.83 mcg/spray</td>
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<td>(may titrate to 1.66 mcg after</td>
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<td>at least 7 days with normal sodium</td>
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<td></td>
<td></td>
<td>levels)</td>
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</table>

VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desmopressin injection (DDAVP)</td>
<td>Ampules: 4 mcg/mL (1 mL)</td>
</tr>
<tr>
<td></td>
<td>Vials: 4 mcg/mL (10 mL)</td>
</tr>
<tr>
<td>Desmopressin nasal spray (Stimate)</td>
<td>Bottle with spray pump: 25 sprays of 150 mcg (2.5 mL)</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Availability</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Desmopressin sublingual tablet (Nocdurna)</td>
<td>Sublingual tablets: 27.7 mcg, 55.3 mcg</td>
</tr>
<tr>
<td>Desmopressin nasal spray (Noctiva)</td>
<td>Nasal spray: 3.5 mL bottle (30 effective 0.1 mL doses of either 0.83 mcg or 1.66 mcg)</td>
</tr>
</tbody>
</table>

VII. References

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.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>J2597</td>
<td>Injection, desmopressin acetate, per 1 mcg</td>
</tr>
<tr>
<td>Reviews, Revisions, and Approvals</td>
<td>Date</td>
</tr>
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<td>----------------------------------</td>
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<tr>
<td>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.</td>
<td>04.01.16</td>
</tr>
<tr>
<td>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. Wording for uses and approval periods for all blood factor products made consistent across all policies. Efficacy statement added to renewal criteria. Hemophiliacs are specified as “congenital” versus “acquired” across blood factor policies where indicated. Reviewed by specialist-hematology/internal medicine</td>
<td>04.01.17</td>
</tr>
</tbody>
</table>
| 1Q18 Annual Review  
- Policies combined for Centene Medicaid and Marketplace lines of business. Marketplace policy included Stimate.  
- 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             |
| 1Q 2019 annual review: no significant changes; references reviewed and updated. | 09.26.18   | 02.19             |
| No significant changes; added Nocturna to policy per SDC and prior approved clinical guidance. | 02.01.19   |                   |
| 1Q 2020 annual review: no significant changes; references reviewed and updated. | 10.29.19   | 02.20             |

**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.

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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.

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