Clinical Policy: Desmopressin Acetate (DDAVP, Noctiva, Stimate)
Reference Number: CP.HNMC.01
Effective Date: 11.16.16
Last Review Date: 11.17
Line of Business: Medicaid – Medi-Cal

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

Description
Desmopressin acetate (DDAVP®, Noctiva®, Stimate®) is a synthetic analog of the natural pituitary hormone arginine vasopressin, an antidiuretic hormone affecting renal water conservation.

FDA approved indication
Primary Nocturnal Enuresis (DDAVP Tablet ONLY):
• May be used alone or as an adjunct to behavioral conditioning or other non-pharmacologic intervention

Central Cranial Diabetes Insipidus (DDAVP Nasal Spray, Rhinal Tube, Injection, Tablet):
• As antidiuretic replacement therapy in the management of central cranial (neurogenic) diabetes insipidus and for management of the temporary polyuria and polydipsia following head trauma or surgery in the pituitary region. Ineffective for the treatment of nephrogenic diabetes insipidus.

Nocturia due to nocturnal polyuria (Noctiva ONLY):
• For the treatment of nocturia due to nocturnal polyuria in adults who awaken at least 2 times per night to void

Hemophilia A (DDAVP Injection, Stimate Nasal Spray):
• For patients with Hemophilia A with Factor VIII coagulant activity levels greater than 5%.
• DDAVP will often maintain hemostasis in patients with hemophilia A during surgical procedures and postoperatively when administered 30 minutes prior to scheduled procedure.
• DDAVP will also stop bleeding in hemophilia A patients with episodes of spontaneous or trauma-induced injuries such as hemarthroses, intramuscular hematomas or mucosal bleeding.

von Willebrand's Disease (Type I) (DDAVP Injection, Stimate Nasal Spray):
• For patients with mild-to-moderate classic von Willebrand's disease (Type I) with Factor VIII levels greater than 5%.
• DDAVP will usually stop bleeding in mild to moderate von Willebrand’s patients with episodes of spontaneous or trauma-induced injuries such as hemarthroses, intramuscular hematomas or mucosal bleeding.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria
It is the policy of health plans affiliated with Centene Corporation® that desmopressin acetate is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Primary Nocturnal Enuresis (must meet all):
      1. Diagnosis of primary nocturnal enuresis;
      2. Request is for DDAVP tablets;
      3. Failure of at least a three month trial of bed-wetting monitor;
      4. Dose does not exceed 0.6 mg/day.
   
   Approval duration: One year

   B. Central Cranial Diabetes Insipidus (must meet all):
      1. Diagnosis of central cranial diabetes insipidus;
      2. Request is for DDAVP;
      3. If under 21 years of age, redirect to California Children’s Services (CCS);
      4. Dose does not exceed: Tablet – 1.2 mg/day; Nasal spray/rhinal tube – 40 mcg/day;
         Injection – 8 mcg/day.
   
   Approval duration: Length of Benefit

   C. Hemophilia A, von Willebrand’s disease (Type I) (must meet all):
      1. Diagnosis of Hemophilia A or von Willebrand’s disease (Type I);
      2. Request is for DDAVP injection of Stimate;
      3. For Stimate requests, dose does not exceed 300 mcg/day.
   
   Approval duration: Length of Benefit

   D. Nocturia (must meet all):
      1. Diagnosis of nocturia due to nocturnal polyuria;
      2. Request is for Noctiva;
      3. Request is for an adult patient;
      4. Dose does not exceed 1.66 mcg/day.
   
   Approval duration: Length of Benefit

   E. Other diagnoses/indications
      1. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III
         (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy
   A. All Indications (must meet all):
      1. Currently receiving medication via a health plan affiliated with Centene Corporation
         or member has previously met initial approval criteria;
      2. Member is responding positively to therapy [e.g., reduction in bed wetting, bleeding,
         nocturia episodes];
      3. If request is for a dose increase, new dose does not exceed:
         a. DDAVP tablets – 1.2 mg/day, nasal spray/rhinal tube – 40 mcg/day
         b. Noctiva – 1.66 mcg/day
         c. Stimate – 300 mcg/day
Approval duration: Primary Nocturnal Enuresis – One year; All other indications - Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via a health plan affiliated with Centene Corporation and documentation supports positive response to therapy.
      Approval duration: Duration of request or 12 months (whichever is less); or
   2. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

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 policy – CP.PMN.53 or evidence of coverage documents
   B. Primary Nocturnal Enuresis (DDAVP Nasal Spray, Rhinal Tube, Noctiva);
   C. Patients with hyponatremia or a history of hyponatremia;
   D. Treatment of nephrogenic diabetes insipidus;
   E. 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 Rhinal Tube, Stimate Nasal Spray);
   F. The treatment of severe classic von Willebrand’s disease (Type I) and when there is evidence of an abnormal molecular form of factor VIII antigen (Injection).

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   CCS: California Children’s Services

   Appendix B: General Information
   • In December, 2007, Sanofi Aventis sent a letter to healthcare professionals stating that the nasal spray and rhinal tube formulations of DDAVP are no longer indicated for Primary Nocturnal Enuresis. There was also a warning and precaution regarding hyponatremia, fluid restriction, and a recommendation to supervise administration in children. Unless properly diagnosed and treated, hyponatremia can be fatal.
   • Per the package insert, DDAVP is ineffective for the treatment of nephrogenic diabetes insipidus.
   • Per the package insert, Stimate should not be used to treat patients with Type IIB von Willebrand's disease since platelet aggregation may be induced.
   • Per package insert, DDAVP Rhinal Tube and Stimate Nasal Spray 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.
   • Per package insert, DDAVP Injection is not indicated for the treatment of severe classic von Willebrand’s disease (Type I) and when there is evidence of an abnormal molecular form of factor VIII antigen.
• Micromedex Class IIa for a urine concentration test. Intranasal desmopressin (20-40 mcg) is an adequate alternative to vasopressin for testing maximal renal concentrating capacity.
• 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.

Appendix C: Therapeutic Alternatives

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imipramine HCL</td>
<td>Nocturnal Enuresis: Age 6 to 12 years: 25 to 50 mg PO 1 hour before bedtime Age &gt;12 years: 25 to 75 mg PO 1 hour before bedtime (increase in 25 mg increments to max dose of 2.5 mg/kg/day)</td>
<td>A dose &gt; 75 mg/day does not enhance efficacy and increases side effects.</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.

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>DDAVP [tablet/oral]</td>
<td>Primary Nocturnal Enuresis</td>
<td>Age 6 years and older: 0.2 to 0.6 mg PO QHS</td>
<td>1.2 mg/day</td>
</tr>
<tr>
<td>DDAVP [tablet/oral]</td>
<td>Central Diabetes Insipidus</td>
<td>Adults and Children: 0.05 mg (1/2 of the 0.1 mg tablet) PO BID (individually adjuste dose to optimum therapeutic dose) Range: 0.1 to 1.2 mg PO in two or three divided doses</td>
<td>1.2 mg/day</td>
</tr>
<tr>
<td>DDAVP [nasal spray, rhinal tube]</td>
<td>Central Cranial Diabetes Insipidus</td>
<td>Adults: 0.2 mL (20 mcg) INTRANASALLY BID [range: 0.1 to 0.4 mL (10 to 40 mcg) INTRANASALLY as single dose or in divided doses, up to TID]</td>
<td>40 mcg/day</td>
</tr>
<tr>
<td>Drug</td>
<td>Condition</td>
<td>Dosage</td>
<td><em>q</em> per Day</td>
</tr>
<tr>
<td>------------------------------</td>
<td>------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
<td>------------</td>
</tr>
<tr>
<td><strong>DDAVP [injection]</strong></td>
<td>Diabetes Insipidus</td>
<td>Adults: 0.5 to 1 mL (2 to 4 mcg) SC/IV BID</td>
<td>8 mcg/day</td>
</tr>
<tr>
<td><strong>DDAVP [injection]</strong></td>
<td>Hemophilia A and von Willebrand’s Disease (Type I)</td>
<td>0.3 mcg/kg IV over 15 to 30 minutes (dilute in 50 mL of sterile physiological saline and infused slowly)</td>
<td>N/A</td>
</tr>
</tbody>
</table>
| **Stimate [nasal spray]**   | Hemophilia A and von Willebrand’s Disease (Type I) | Weight ≥50 kg: 1 spray (150 mcg) into each nostril QD (total dose 300 mcg, 1 spray = 0.1 mL = 150 mcg)  
Weight <50 kg: 1 spray (150 mcg) into one nostril QD | 300 mcg/day |
| **Noctiva**                  | Nocturia Due to Nocturnal Polyuria              | Patients under 65 years old without increased risk for hyponatremia: One 1.66 mcg spray in either nostril 30 minutes before bedtime  
Patients 65 and older or younger patients at risk for hyponatremia: 0.83 mcg nightly. If needed, dose may be titrated to 1.66 mcg after at least 7 days with normal serum sodium | 1.66 mcg/day |
VI. Product Availability

<table>
<thead>
<tr>
<th>Drug</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDAVP Tablet</td>
<td>0.1 mg and 0.2 mg</td>
</tr>
<tr>
<td>DDAVP Nasal Spray</td>
<td>5 mL bottle (50 sprays of 10 mcg)</td>
</tr>
<tr>
<td>DDAVP Rhinal Tube</td>
<td>Calibrated at 0.2, 0.15, 0.1 and 0.05 mL doses; 2.5 mL bottle</td>
</tr>
<tr>
<td>DDAVP Injection</td>
<td>4 mcg/mL in 1 mL single-dose vial and 10 mL multi-dose vial</td>
</tr>
<tr>
<td>Stimate Nasal Spray</td>
<td>2.5 mL bottle (25 sprays of 150 mcg)</td>
</tr>
<tr>
<td>Noctiva Nasal Spray</td>
<td>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

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Converted to new template. Added Noctiva to policy.</td>
<td>05.17</td>
<td>08.17</td>
</tr>
<tr>
<td>Minor changes to verbiage and grammar. References updated.</td>
<td>10.05.17</td>
<td>11.17</td>
</tr>
</tbody>
</table>

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.

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