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

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.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 ≥ 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: 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: 6 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: 6 months

D. **Nocturia** (must meet all):
1. Diagnosis of nocturia due to nocturnal polyuria;
2. Age ≥ 18 years;
3. Request is for Noctiva;
4. Dose does not exceed 1.66 mcg per day (1 bottle per 30 days).

Approval duration: 12 months

E. **Other diagnoses/indications**
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. **Continued Therapy**

A. **All Indications in Section I** (must meet all):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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. Noctiva: 1.66 mcg per day (1 bottle per 30 days).

Approval duration: 12 months

B. **Other diagnoses/indications** (must meet 1 or 2):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy. 
   Approval duration: Duration of request or 6 months (whichever is less); or 
2. Refer to ERX.PA.01 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 – ERX.PA.01 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; comitant 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 antiuretic 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):
  o DDAVP injection, Stimate: none reported 
  o 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 insipidus</td>
<td>2 to 4 mcg IV or SC daily, usually in 2 divided doses</td>
<td>4 mcg/day</td>
</tr>
<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>
</tbody>
</table>
| 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 |

VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
</table>
| 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

Reviews, Revisions, and Approvals | Date | P&T Approval Date
--- | --- | ---
Policy created | 04.17 | 08.17
3Q 2018 annual review: no significant changes; references reviewed and updated. | 06.27.18 | 08.18
Added criteria for DDAVP injection and Stimate; references reviewed and updated. | 07.09.18 | 11.18
1Q 2019 annual review: no significant changes; references reviewed and updated. | 09.26.18 | 02.19

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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 policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

©2017 Envolve Pharmacy Solutions. All rights reserved. All materials are exclusively owned by Envolve Pharmacy Solutions and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Envolve Pharmacy Solutions. You may not alter or remove any trademark, copyright or other notice contained herein.