Clinical Policy: Desmopressin Acetate (DDAVP Injection, Stimate)

Reference Number: CP.PHAR.214
Effective Date: 05.01.16
Last Review Date: 02.18 Coding Implications
Line of Business: Health Insurance Marketplace, Medicaid Revision Log

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

Description
Desmopressin acetate (DDAVP®, Stimate®) is a synthetic analog of the natural pituitary hormone 8-arginine vasopressin (ADH), an antidiuretic hormone.

FDA Approved Indication(s)
DDAVP injection is 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
- For the treatment of patients with mild to moderate classic von Willebrand's disease (Type I) with factor VIII levels greater than 5%
- For the treatment of patients with hemophilia A with factor VIII coagulant activity levels greater than 5%

Limitation(s) of use:

- DDAVP is 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 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.
- DDAVP is ineffective for the treatment of nephrogenic diabetes insipidus.

Stimate nasal spray is indicated:

- For the treatment of patients with hemophilia A with Factor VIII coagulant activity levels greater than 5%
- For the treatment of patients with mild to moderate classic von Willebrand’s disease (Type I) with Factor VIII levels greater than 5%

Limitation(s) of use:

- Stimate is 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 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.

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 DDAVP injection or Stimate is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Polyuria and Central Diabetes Insipidus (must meet all)**:**
1. Diagnosis of central diabetes insipidus;
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 12 years;
4. Request is for DDAVP injection;
5. Failure of a trial of desmopressin tablets, unless contraindicated or clinically significant adverse effects are experienced, or documentation that the member is unable to swallow tablets;
6. Prescribed as antidiuretic replacement therapy for one of the following conditions:
   a. Central (cranial) diabetes insipidus;
   b. Temporary polyuria and polydipsia following head trauma or surgery in the pituitary region;
7. Creatinine clearance is ≥ 50 mL/min and serum sodium concentration is ≥ 35 meq/L;
8. Dose does not exceed 4 mcg/day injection.

Medicaid- 6 months
Health Insurance Marketplace - 12 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 one of the following:
   a. Control and prevention of bleeding episodes;
   b. Perioperative management;
   c. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes;
5. Does not have factor VIII antibodies;
6. Factor VIII coagulant activity levels are >5%;
7. For DDAVP injection requests: Creatinine clearance is ≥ 50 mL/min and serum sodium concentration is ≥ 35 meq/L;
8. Dose does not exceed the following (a or b):
   a. DDAVP injection: 0.3 mcg/kg per dose;
   b. Stimate: 300 mcg/day.

Medicaid- 6 months
Health Insurance Marketplace – 12 months

C. Von Willebrand Disease (must meet all)**:**
1. Diagnosis of von Willebrand disease (VWD), Type 1 or Type 2;
2. Prescribed by or in consultation with a hematologist;

3. Age ≥ 3 months;
4. Factor VIII coagulant activity levels are >5%;
5. Request is for one of the following:
   a. Control and prevention of bleeding episodes;
   b. Perioperative management;
   c. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes;
6. For DDAVP injection requests: Creatinine clearance is ≥ 50 mL/min and serum sodium concentration is ≥ 35 meq/L;
7. Dose does not exceed the following (a or b):
   a. DDAVP injection: 0.3 mcg/kg per dose;
   b. Stimate: 300 mcg/day.

Medicaid- 6 months
Health Insurance Marketplace – 12 months

D. 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): 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 all initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed the following (a or b):
   a. DDAVP injection: 4 mcg/day for diabetes insipidus and 0.3 mcg/kg per dose for hemophilia A or VWD;
   b. Stimate: 300 mcg/day.

Medicaid- 6 months
Health Insurance Marketplace – 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 for specialty 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): 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 –

HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

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 (DDAVP®) oral tablets	0.05 mg orally twice daily, titrated to a maintenance dose in the range of 0.1 mg to 1.2 mg divided into two or three 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.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
desmopressin (DDAVP®) injection	Central diabetes insipidus	2 to 4 mcg daily, administered IV or SC, usually in two divided doses	4 mcg/day
desmopressin (DDAVP®) injection	Hemophilia A and von Willebrand's disease	0.3 mcg/kg IV or SC as needed	0.3 mcg/kg/dose
Stimate® (desmopressin) nasal spray	Hemophilia A and von Willebrand's disease	One spray per nostril, for a total dose of 300 mcg	300 mcg/dose

VI. Product Availability

Drug Name	Availability
desmopressin (DDAVP®) injection	Ampules: 4 mcg/mL (1 mL) Vials: 4 mcg/mL (10 mL)
Stimate® (desmopressin) nasal spray	Bottle with spray pump: 25 sprays of 150 mcg (2.5 mL)

VII. References

1. DDAVP Injection Prescribing Information. Parsippany, NJ: Ferring Pharmaceuticals; April 2015. Available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=651f6fee-a2c7-431b-8d5d-58b156c72244. Accessed November 29, 2017.
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 November 29, 2017.
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.

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. Wording for uses and approval periods for all blood factor products made consistent across all policies. Efficacy statement added to renewal criteria.	04.01.17	05.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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 Medicaid and HIM lines of business. -No significant changes -Converted to new template - Marketplace policy included Stimate, therefore Stimate remains in the policy. - Added age limit for diabetes insipidus. - References reviewed and updated	11.29.17	02.18

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.