

## Desmopressin: Drug information

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(For additional information [see "Desmopressin: Patient drug information"](#) and [see "Desmopressin: Pediatric drug information"](#))

For abbreviations and symbols that may be used in Lexicomp ([show table](#))

**Brand Names: U.S.** DDAVP; DDAVP Rhinal Tube; Stimate

**Brand Names: Canada** Apo-Desmopressin®; DDAVP®; DDAVP® Melt; Minirin®; Novo-Desmopressin; Octostim®; PMS-Desmopressin

**Pharmacologic Category** Antihemophilic Agent; Hemostatic Agent; Hormone, Posterior Pituitary; Vasopressin Analog, Synthetic

### Dosing: Adult

#### Diabetes insipidus:

*I.V., SubQ:* U.S. labeling: 2-4 mcg/day (0.5-1 mL) in 2 divided doses or one-tenth (1/10) of the maintenance intranasal dose. Fluid restriction should be observed.

*I.M., I.V., SubQ:* Canadian labeling (not in U.S. labeling): 1-4 mcg (0.25-1 mL) once daily or one-tenth (1/10) of the maintenance intranasal dose. Fluid restriction should be observed.

*Intranasal (100 mcg/mL nasal solution):* 10-40 mcg/day (0.1-0.4 mL) divided 1-3 times/day; adjust morning and evening doses separately for an adequate diurnal rhythm of water turnover. **Note:** The nasal spray pump can only deliver doses of 10 mcg (0.1 mL) or multiples of 10 mcg (0.1 mL); if doses other than this are needed, the rhinal tube delivery system is preferred. Fluid restriction should be observed.

#### Oral:

U.S. labeling: Initial: 0.05 mg twice daily; total daily dose should be increased or decreased as needed to obtain adequate antidiuresis (range: 0.1-1.2 mg divided 2-3 times/day). Fluid restriction should be observed.

Canadian labeling (not in U.S. labeling): Initial: 0.1 mg 3 times/day; total daily dose should be increased or decreased as needed to obtain adequate antidiuresis (range: 0.3-1.2 mg divided 3 times/day).

Fluid restriction should be observed.

*Sublingual formulation:* Canadian labeling (not in U.S. labeling): Initial: 60 mcg 3 times/day; total daily dose should be increased or decreased as needed to obtain adequate antidiuresis. Usual maintenance: 60-120 mcg 3 times/day (range: 120-720 mcg divided 2-3 times/day). Fluid restriction should be observed.

**Nocturnal enuresis:** *Oral:* 0.2 mg at bedtime; dose may be titrated up to 0.6 mg to achieve desired response.

**Hemophilia A and mild-to-moderate von Willebrand disease (type 1):**

*I.V.:* 0.3 mcg/kg by slow infusion; if used preoperatively, administer 30 minutes before procedure

Canadian labeling (not in U.S. labeling): Maximum I.V. dose: 20 mcg

*Intranasal (using high concentration spray [1.5 mg/mL]):* <50 kg: 150 mcg (1 spray); >50 kg: 300 mcg (1 spray each nostril); repeat use is determined by the patient's clinical condition and laboratory work. If using preoperatively, administer 2 hours before surgery.

**Uremic bleeding associated with acute or chronic renal failure (unlabeled use)** (Watson, 1984): *I.V.:* 0.4 mcg/kg over 10 minutes

**Prevention of surgical bleeding in patients with uremia (unlabeled use)** (Mannucci, 1983): *I.V.:* 0.3 mcg/kg over 30 minutes

**Dosing: Pediatric**

(For additional information [see "Desmopressin: Pediatric drug information"](#))

**Diabetes insipidus:**

*I.M., I.V., SubQ:* Canadian labeling (not in U.S. labeling): Infants and Children  $\geq$ 3 months: 0.4 mcg (0.1 mL) once daily or one-tenth (1/10) of the maintenance intranasal dose. Fluid restriction should be observed.

*I.V., SubQ:*

Children <12 years: No definitive dosing available. Adult dosing should **not** be used in this age group; adverse events such as hyponatremia-induced seizures may occur. Dose should be reduced. Some have suggested an initial dosage range of 0.1-1 mcg in 1 or 2 divided doses (Cheetham, 2002). Initiate at low dose and increase as necessary. Closely monitor serum sodium levels and urine output; fluid restriction is recommended.

Children  $\geq 12$  years: Refer to adult dosing.

*Intranasal (using 100 mcg/mL nasal solution):*

Infants and Children 3 months to 12 years: Initial: 5 mcg/day (0.05 mL/day) divided 1-2 times/day; range: 5-30 mcg/day (0.05-0.3 mL/day) divided 1-2 times/day; adjust morning and evening doses separately for an adequate diurnal rhythm of water turnover. **Note:** The nasal spray pump can only deliver doses of 10 mcg (0.1 mL) or multiples of 10 mcg (0.1 mL); if doses other than this are needed, the rhinal tube delivery system is preferred. Fluid restriction should be observed.

Children  $\geq 12$  years: Refer to adult dosing.

*Oral:*

U.S. labeling: Children  $\geq 4$  years: Initial: 0.05 mg twice daily; total daily dose should be increased or decreased as needed to obtain adequate antidiuresis (range: 0.1-1.2 mg divided 2-3 times/day). Fluid restriction should be observed.

Canadian labeling (not in U.S. labeling): Children  $\geq 5$  years: Initial: 0.1 mg 3 times/day; total daily dose should be increased or decreased as needed to obtain adequate antidiuresis (range: 0.3-1.2 mg divided 3 times/day). Divide daily doses so that the evening dose is 2 times higher than the morning or afternoon dose to ensure adequate antidiuresis during the night. Fluid restriction should be observed.

*Sublingual formulation:* Canadian labeling (not in U.S. labeling): Infants and Children  $\geq 3$  months: Initial: 60 mcg 3 times/day; total daily dose should be increased or decreased as needed to obtain adequate antidiuresis. Usual maintenance: 60-120 mcg 3 times/day (range: 120-720 mcg divided 2-3 times/day); divide daily doses so that the evening dose is 2 times higher than the morning or afternoon dose to ensure adequate antidiuresis during the night. Fluid restriction should be observed.

### **Hemophilia A and von Willebrand disease (type 1):**

*I.V.:* Infants and Children  $\geq 3$  months: 0.3 mcg/kg by slow infusion; may repeat dose if needed; if used preoperatively, administer 30 minutes before procedure

Canadian labeling (not in U.S. labeling): Maximum I.V. dose: 20 mcg

**Note:** Adverse events such as hyponatremia-induced seizures have

been reported especially in young children using this dosing regimen (Das, 2005; Molnar, 2005; Smith, 1989; Thumfart, 2005; Weinstein, 1989). Fluid restriction and careful monitoring of serum sodium levels and urine output are necessary.

*Intranasal (using high concentration spray [1.5 mg/mL]):* Infants and Children  $\geq 11$  months: Refer to adult dosing.

### **Nocturnal enuresis:**

#### *Oral:*

Children  $\geq 6$  years: 0.2 mg at bedtime. Dose may be titrated up to 0.6 mg to achieve desired response. Fluid intake should be limited 1 hour prior to dose until the next morning, or at least 8 hours after administration. **Note:** In the Canadian labeling, use is approved for patients  $\geq 5$  years.

Children  $> 12$  years: Refer to adult dosing.

*Sublingual:* Canadian labeling (not in U.S. labeling): Children  $\geq 5$  years: Initial: 120 mcg at bedtime; dose may be titrated up to 360 mcg to achieve desired response. Fluid intake should be limited 1 hour prior to dose until the next morning, or at least 8 hours after administration.

**Dosing: Renal Impairment** CrCl  $< 50$  mL/minute: Use is contraindicated according to the manufacturer; however, has been used in acute and chronic renal failure patients experiencing uremic bleeding or for prevention of surgical bleeding (unlabeled uses) (Mannucci, 1983; Watson, 1984).

**Dosing: Hepatic Impairment** No dosage adjustment provided in manufacturer's labeling.

**Dosage Forms: U.S.** Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Injection, as acetate:

DDAVP: 4 mcg/mL (1 mL, 10 mL)

Generic: 4 mcg/mL (1 mL, 10 mL)

Solution, Nasal, as acetate:

DDAVP: 0.01% (5 mL)

DDAVP Rhinal Tube: 0.01% (2.5 mL)

Stimate: 1.5 mg/mL (2.5 mL) [contains benzalkonium chloride]

Generic: 0.01% (2.5 mL, 5 mL)

Tablet, Oral, as acetate:

DDAVP: 0.1 mg, 0.2 mg [scored]

Generic: 0.1 mg, 0.2 mg

## Dosage Forms Considerations

DDAVP and Minirin 5 mL bottles contain 50 sprays.

Stimate 2.5 mL bottles contain 25 sprays.

**Generic Equivalent Available: U.S.** Yes

## Administration

### I.M., I.V. push, SubQ injection:

Central diabetes insipidus: Withdraw dose from ampul into appropriate syringe size (eg, insulin syringe). Further dilution is not required. Administer as direct injection.

### I.V. infusion:

Hemophilia A, von Willebrand disease (type 1), and prevention of surgical bleeding in patients with uremia (unlabeled) (Mannucci, 1983): Infuse over 15-30 minutes

Acute uremic bleeding (unlabeled) (Watson, 1984): May infuse over 10 minutes

### Intranasal:

DDAVP®: Nasal pump spray: Delivers 0.1 mL (10 mcg); for doses <10 mcg or for other doses which are not multiples, use rhinal tube. DDAVP® Nasal spray delivers fifty 10 mcg doses. For 10 mcg dose, administer in one nostril. Any solution remaining after 50 doses should be discarded. Pump must be primed prior to first use.

DDAVP® Rhinal tube: Insert top of dropper into tube (arrow marked end) in downward position. Squeeze dropper until solution reaches desired calibration mark. Disconnect dropper. Grasp the tube 3/4 inch from the end and insert tube into nostril until the fingertips reach the nostril. Place opposite end of tube into the mouth (holding breath). Tilt head back and blow with a strong, short puff into the nostril (for very young patients, an adult should blow solution into the child's nose). Reseal

dropper after use.

**Compatibility** Stable in NS.

## Use

Injection: Treatment of diabetes insipidus; maintenance of hemostasis and control of bleeding in hemophilia A with factor VIII coagulant activity levels >5% and mild-to-moderate classic von Willebrand's disease (type 1) with factor VIII coagulant activity levels >5%

Nasal solutions (DDAVP® Nasal Spray and DDAVP® Rhinal Tube): Treatment of central diabetes insipidus

Nasal spray (Stimate®): Maintenance of hemostasis and control of bleeding in hemophilia A with factor VIII coagulant activity levels >5% and mild-to-moderate classic von Willebrand's disease (type 1) with factor VIII coagulant activity levels >5%

Tablet: Treatment of central diabetes insipidus, temporary polyuria and polydipsia following pituitary surgery or head trauma, primary nocturnal enuresis

**Use - Unlabeled** Uremic bleeding associated with acute or chronic renal failure; prevention of surgical bleeding in patients with uremia

## Adverse Reactions Significant

Frequency may not be defined (may be dose or route related).

Cardiovascular: Blood pressure increased/decreased (I.V.), facial flushing

Central nervous system: Headache (2% to 5%), dizziness (intranasal; ≤3%), chills (intranasal; 2%)

Dermatologic: Rash

Endocrine & metabolic: Hyponatremia, water intoxication

Gastrointestinal: Abdominal pain (intranasal; 2%), gastrointestinal disorder (intranasal; ≤2%), nausea (intranasal; ≤2%), abdominal cramps, sore throat

Hepatic: Transient increases in liver transaminases (associated primarily with tablets)

Local: Injection: Burning pain, erythema, and swelling at the injection site

Neuromuscular & Skeletal: Weakness (intranasal; ≤2%)

Ocular: Conjunctivitis (intranasal; ≤2%), eye edema (intranasal; ≤2%), lacrimation disorder (intranasal; ≤2%)

Respiratory: Rhinitis (intranasal; 3% to 8%), epistaxis (intranasal; ≤3%), nostril

pain (intranasal;  $\leq 2\%$ ), cough, nasal congestion, upper respiratory infection

<1% (Limited to important or life-threatening): Acute cerebrovascular thrombosis (I.V.), acute MI (I.V.), agitation, allergic reactions (rare), anaphylaxis (rare), balanitis, chest pain, coma, diarrhea, dyspepsia, edema, insomnia, itching eyes, light-sensitive eyes, pain, palpitation, seizure, somnolence, tachycardia, thinking abnormal, vomiting, vulval pain, warmth

**Contraindications** Hypersensitivity to desmopressin or any component of the formulation; hyponatremia or a history of hyponatremia; moderate-to-severe renal impairment ( $\text{CrCl} < 50 \text{ mL/minute}$ )

## Warnings/Precautions

### ***Concerns related to adverse effects:***

- Allergic reactions (injectable and intranasal formulations): Severe reactions resembling hypersensitivity (eg, anaphylaxis) reactions have occurred rarely with I.V. and intranasal administration.
- Hyponatremia: Use may rarely lead to hyponatremia and extreme decreases in plasma osmolality, resulting in seizures, coma, and death. Risk factors for hyponatremia with desmopressin use include cystic fibrosis, renal dysfunction, heart failure, young age, advanced age, inappropriate high fluid intake with desmopressin administration, a larger than recommended dose, and concomitant use of medications known to either increase thirst or cause syndrome of inappropriate ADH secretion (SIADH). Fluid restriction during use is recommended.
- Thrombotic events: Acute cerebrovascular thrombosis and acute myocardial infarction have occurred (rare); use with caution in patients predisposed to thrombus formation.

### ***Disease-related concerns:***

- Cardiovascular disease: Use with caution in patients with coronary artery insufficiency or hypertensive cardiovascular disease; may increase or decrease blood pressure leading to changes in heart rate.
- Polydipsia (habitual or psychogenic): Use with caution in patients with habitual or psychogenic polydipsia. These patients are at greater risk of hyponatremia. Use in these patients is contraindicated in Canadian labeling.
- von Willebrand's disease type 2B: Patients with type 2B von Willebrand's disease requiring hemostasis should not be treated with desmopressin

since use may result in platelet aggregation, thrombocytopenia, and possibly thrombosis.

***Special populations:***

- Elderly: Fluid intake should be adjusted downward in the elderly to decrease the possibility of water intoxication and hyponatremia.
- Pediatrics: Fluid intake should be adjusted downward in very young patients to decrease the possibility of water intoxication and hyponatremia.

***Dosage form specific issues:***

- Injection and high concentration spray (1.5 mg/mL): Not for use in hemophilia B, type 2B von Willebrand disease, severe classic von Willebrand disease (type 1), or in patients with factor VIII antibodies. In general, the injection and high concentration spray are also not recommended for use in patients with  $\leq 5\%$  factor VIII activity level, although it may be considered in selected patients with activity levels between 2% and 5%.
- Intranasal: Consider alternative route of administration (I.V.) if changes in the nasal mucosa (scarring, edema) occur leading to unreliable absorption.
- Tablet: Patients should be instructed to restrict fluid intake from 1 hour before to 8 hours after taking desmopressin tablets. Consider alternative route of administration (I.V. or intranasal) with inadequate therapeutic response at maximum recommended oral doses.

***Appropriate use:***

- Interruption of therapy: Therapy should be interrupted if the patient experiences an acute illness (eg, fever, recurrent vomiting or diarrhea), vigorous exercise, or any condition associated with an increase in water consumption.

***Other warnings/precautions:***

- Long-term effects: Some patients may demonstrate a change in response after long-term therapy (>6 months) characterized as decreased response or a shorter duration of response.

**Metabolism/Transport Effects** None known.

**Drug Interactions**

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Analgesics (Opioid): May enhance the adverse/toxic effect of Desmopressin.  
*Risk C: Monitor therapy*

Carbamazepine: May enhance the adverse/toxic effect of Desmopressin. *Risk C: Monitor therapy*

Chlorpromazine: May enhance the adverse/toxic effect of Desmopressin. *Risk C: Monitor therapy*

Demeclocycline: May diminish the therapeutic effect of Desmopressin. *Risk C: Monitor therapy*

Lamotrigine: May enhance the adverse/toxic effect of Desmopressin. *Risk C: Monitor therapy*

Lithium: May diminish the therapeutic effect of Desmopressin. Desmopressin may increase the serum concentration of Lithium. *Risk C: Monitor therapy*

Nonsteroidal Anti-Inflammatory Agents: May enhance the adverse/toxic effect of Desmopressin. *Risk C: Monitor therapy*

Selective Serotonin Reuptake Inhibitors: May enhance the adverse/toxic effect of Desmopressin. *Risk C: Monitor therapy*

Tricyclic Antidepressants: May enhance the adverse/toxic effect of Desmopressin. *Risk C: Monitor therapy*

## **Pregnancy Risk Factor B** ([show table](#))

**Pregnancy Implications** Adverse events were not observed in animal reproduction studies. Anecdotal reports suggest congenital anomalies and low birth weight. However, causal relationship has not been established.

Desmopressin has been used safely throughout pregnancy for the treatment of diabetes insipidus (Brewster, 2005; Schrier, 2010). The use of desmopressin is limited for the treatment of von Willebrand disease in pregnant women (NHLBI, 2007).

**Lactation** Excretion in breast milk unknown/use caution

**Breast-Feeding Considerations** It is not known if desmopressin is excreted in breast milk. The manufacturer recommends that caution be exercised

when administering desmopressin to nursing women.

## **Pricing: U.S.**

**Solution** (DDAVP Injection)

4 mcg/mL (1 mL): \$65.81

**Monitoring Parameters** Blood pressure and pulse should be monitored during I.V. infusion

**Note:** For all indications, fluid intake, urine volume, and signs and symptoms of hyponatremia should be closely monitored especially in high-risk patient subgroups (eg, young children, elderly, patients with heart failure).

Diabetes insipidus: Urine specific gravity, plasma and urine osmolality, serum electrolytes

Hemophilia A: Factor VIII coagulant activity, factor VIII ristocetin cofactor activity, and factor VIII antigen levels, aPTT

von Willebrand disease: Factor VIII coagulant activity, factor VIII ristocetin cofactor activity, and factor VIII von Willebrand antigen levels, bleeding time

Nocturnal enuresis: Serum electrolytes if used for >7 days

**Mechanism of Action** In a dose dependent manner, desmopressin increases cyclic adenosine monophosphate (cAMP) in renal tubular cells which increases water permeability resulting in decreased urine volume and increased urine osmolality; increases plasma levels of von Willebrand factor, factor VIII, and t-PA contributing to a shortened activated partial thromboplastin time (aPTT) and bleeding time.

## **Pharmacodynamics/Kinetics**

Onset of action:

Intranasal: Antidiuretic: 15-30 minutes; Increased factor VIII and von Willebrand factor (vWF) activity (dose related): 30 minutes

Peak effect: Antidiuretic: 1 hour; Increased factor VIII and vWF activity: 1.5 hours

**I.V. infusion: Increased factor VIII and vWF activity: 30 minutes (dose related)**

### Peak effect: 1.5-2 hours

Oral tablet: Antidiuretic: ~1 hour

Peak effect: 4-7 hours

Duration: Intranasal, I.V. infusion, Oral tablet: ~6-14 hours

Absorption: Sublingual: Rapid

Bioavailability: Intranasal: ~3.5%; Oral tablet: 5% compared to intranasal, 0.16% compared to I.V.

Half-life elimination: Intranasal: ~3.5 hours; I.V. infusion: 3 hours; Oral tablet: 2-3 hours

Renal impairment: ≤9 hours

Excretion: Urine

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