DDAVP Nasal Spray
(desmopressin acetate)

A better way to deliver DDAVP

Your doctor has prescribed DDAVP as antidiuretic hormone replacement therapy. Follow the dosage schedule that is specified. The convenient nasal spray pump provides an efficient, reliable way to administer your medication. It is important, however, to adhere carefully to the following instructions so that you will always receive a consistent dose of your medication.

CAUTION: The nasal spray pump accurately delivers 50 doses of 10 micrograms each. Any solution remaining after 50 doses should be discarded since the amount delivered thereafter per actuation may be substantially less than 10 micrograms of drug. Do not transfer any remaining solution to another bottle. Please read the following instructions carefully before using the spray pump.

Ensure that in children administration is under adult supervision in order to control the dose intake.

If you accidentally deliver/administer too much of a dose, immediately telephone your doctor or a certified Regional Poison Control Center for advice. In case of overdosage, rare severe allergic reactions have been reported with DDAVP. Anaphylaxis has been reported rarely in association with severe allergic reactions following administration of the nasal spray. Recovery from surgery.

Intranasal DDAVP at high dosage has infrequently produced a slight elevation of blood pressure within 1 minute of administration. The spray should not be used in patients with cerebrovascular accident (stroke), subarachnoid hemorrhage, preeclampsia or eclampsia, advanced heart failure, or aortic or mitral valve incompetence.

To administer a 10-microgram dose, place the spray nozzle in nostril and press the spray pump once. If a higher dose has been prescribed, spray half the dose in each nostril. The spray pump cannot be used for doses less than 10 micrograms or doses other than multiples of 10 micrograms.

4. Replace the protective cap on bottle after use. The pump will stay primed for up to one week. If the product has not been used for a period of one week, re-prime the pump by pressing once.
**DDAVP**<sup>®</sup> Nasal Spray (desmopressin acetate)

5. We have included a convenient check-off chart to assist you in keeping track of medication doses used. This will help assure that you receive 50 (*all doses*) of medication. Please note that the bottle has been filled with extra solution to accommodate the initial priming activity.

**DDAVP Nasal Spray**

**50-Dose Check-off**

1. Retain with medication or affix in convenient location.
2. Starting with dose #1, check off after each administration.
3. Discard medication after 50 doses.

**Store at Controlled Room Temperature 20 to 25°C (68 to 77°F) [see USP].** **STORE BOTTLE IN UPRIGHT POSITION.**

**Manufactured for:**
Ferring Pharmaceuticals Inc.
Parsonsny, NJ 07054 USA

**Rev. 04/2015**

**Parsippany, NJ 07054 USA**

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Ferring Pharmaceuticals Inc.
Parisonsny, NJ 07054 USA

**Rev. 04/2015**

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**WARNINGS**

There are reports of an occasional change in response with time, usually greater than 50%. Some patients may show a decreased responsiveness, others a shortened duration of effect. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function. DDAVP is contraindicated in patients with renal insufficiency (see CLINICAL PHARMACOLOGY, Adverse Events, and CONTRAINDICATIONS).

**OVERDOSAGE**

An oral LD<sub>50</sub> has not been established. An intravenous dose of 2 mg/kg in mice demonstrated no effect.

**ADVERSE REACTIONS**

Signs of overdose may include confusion, drowsiness, altered state, headache, problems with passing urine and weight gain. In a small number of cases, confusion, use of extreme care with the patient to prevent possible hyponatremia and water intoxication. See WARNINGS. The dose must be individually adjusted for the patient with addiction in the very young to the danger of an extreme decrease in plasma osmolality with resulting convulsions. Dose should start at 0.05 mL or less.

**ADVERSE REACTIONS**

**POST-MARKETING**

There have been rare reports of hyponatremic convulsions associated with hyponatremia and water intoxication. (See WARNINGS, The dose must be...)

**ADVERSE REACTIONS**

**POST-MARKETING**

There have been no controlled studies in nursing mothers. A single study in a small number of cases, confusion, use of extreme care with the patient to prevent possible hyponatremia and water intoxication. See WARNINGS. The dose must be individually adjusted for the patient with addiction in the very young to the danger of an extreme decrease in plasma osmolality with resulting convulsions. Dose should start at 0.05 mL or less.

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WARNINGS

1. The intranasal route only.

2. DDAVP Rhinal Tube should only be used where orally administered formulations are not available.

3. Very rare cases of hyponatremia have been reported worldwide postmarketing with intravenous and intranasal administration of DDAVP.

4. Patients are selected for therapy by establishing the diagnosis by means of the water deprivation test, the hypertonic saline infusion test, and/or the response to antidiuretic hormone. Continued therapy in the management of central cranial diabetes insipidus and for management of severe renal polyuria and polydipsia include urine volume and osmolality.

5. Intranasal DDAVP should be used with caution in patients with coronary artery insufficiency and/or hypertensive cardiovascular disease because of the possible rise in blood pressure.

6. DDAVP should be used with caution in patients with habitual or psychogenic polydipsia who may be more likely to drink excessive amounts of water putting them at greater risk of hyponatremia.

7. Intranasal DDAVP at high dosage has infrequently produced a slight elevation of blood pressure, which disappeared with a reduction in dosage. The drug should be used with caution in patients with coronary insufficiency and/or hypertension. In earlier animal studies the rise in blood pressure was attributed to a local inactivation of the peptide. There is no evidence this effect is due to the development of binding antibodies but may be due to a local inactivation of the peptide.

CONTRAINdications

DDAVP is contraindicated in patients with hyponatremia or a history of hyponatremia.

DDAVP is also available as a solution for injection when the intranasal route may be compromised.

General:

1. Intranasal DDAVP should only be used in patients where orally administered formulations are not available.

2. DDAVP is contraindicated in patients with renal failure or severe renal polyuria (defined as a creatinine clearance below 15 ml/min).

3. DDAVP is contraindicated in patients with hypothyroidism or a history of hypothyroidism.

4. Intranasal DDAVP should not be used in patients with known hypersensitivity to desmopressin acetate or any of the components of DDAVP Rhinal Tube.

5. General:

a. Intranasal DDAVP is highly absorbed; therefore, it may not be evident whether dosages are appropriate and should be discussed with the patient and physician.

b. There is no evidence this effect is due to the development of binding antibodies but may be due to a local inactivation of the peptide.

6. Intranasal DDAVP should be used with caution in patients with conditions associated with fluid and electrolyte imbalance, such as cystic fibrosis, heart failure and renal disorders because these conditions are frequent in patients with diabetes insipidus.

7. Pharmacokinetics:

a. 1-(3-mercaptopropionic acid)-8-D-arginine vasopressin monoacetate (salt) trihydrate.

b. DDAVP Rhinal Tube—desmopressin acetate.

3. Very rare cases of hyponatremia have been reported worldwide postmarketing with intravenous and intranasal administration of DDAVP. One mL (3.1 mg) of intranasal DDAVP desmopressin acetate has an antidiuretic activity of about 400 to 10 mg of desmopressin acetate in equivalent to 40 IU.

4. The intranasal half-life has been DDAVP 7.8 and 75.5 minutes for the fast and slow phases, compared with 2.2 and 10 minutes for systemic vasopressin, another form of the hormone used in this condition. As a result, intranasal DDAVP provides a prolonged period of antidiuretic action with a long duration after each administration.

5. The change in structure of arginine vasopressin to DDAVP less resulted in a decreased antidiuretic action and decreased sodium and water renal loss compared to the antidiuretic activity of vasopressin which effectively decreases the plasma osmolality.

6. DDAVP administered intranasally has an antidiuretic effect about one-tenth that of an equivalent dose administered by injection.

7. Intranasal DDAVP should only be used in patients where orally administered formulations are not available.
5. Hold the tube with the fingers approximately ¾ inch from the end and insert into a nostril until the tips of the fingers reach the nostril.

6. Put the other end of the tube into the mouth. Hold the breath, tilt the head back and then blow with a short, strong puff through the tube so that the solution reaches the right place in the nasal cavity. Through this procedure, medication is limited to the nasal cavity and the preparation does not pass down into the throat.

In very young patients, it may be necessary for an adult to blow the solution into the child’s nose. In such cases, the tube will not need to be put into the nose as far as in the other child or adult. The tube should be placed in the nose gently just far enough so that the solution does not run out. A baby must be held firmly and securely.

7. After use, reseal dropper tip and close the bottle with the plastic cap. Wash the tube in water and shake thoroughly, until no more water is left. The tube can then be used for the next application.

**IMPORTANT:** Replace Knurled Seal

Store refrigerated 2 to 8°C (36 to 46°F). When traveling, closed bottles will maintain stability for 3 weeks when stored at controlled room temperature, 20 to 25°C (68 to 77°F).

**WARNINGS**

**Important:** Do not give intranasal DDAVP to patients who have had a previous allergic reaction to desmopressin acetate.

**ADVERSE REACTIONS**

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>PLACEBO</th>
<th>20 mcg</th>
<th>40 mcg</th>
<th>40 mcg (Novo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Pain</td>
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<td>Anemia</td>
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<tr>
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**RESPIRATORY SYSTEM**

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<tbody>
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</tr>
<tr>
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<td>Rhinitis</td>
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<tr>
<td>Rhinorrhea</td>
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**TOTAL** | **20** | **20** | **20** |

**DERMATOLOGY**

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<tr>
<td>pruritus</td>
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<td>0</td>
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</tr>
<tr>
<td>pruritus</td>
<td>0</td>
<td>0</td>
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</tr>
</tbody>
</table>

**TOTAL** | **20** | **20** | **20** |

**SPECIAL SENSIBILITY**

<table>
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<tr>
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<th>20 mcg</th>
<th>40 mcg</th>
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<tbody>
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</tr>
<tr>
<td>Edema Eyes</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lachrymation Disorder</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**TOTAL** | **20** | **20** | **20** |

**NOTES**

- **Post Marketing:** There have been rare reports of hypertensive crises associated with concomitant use of von Willebrand factor and desmopressin acetate.

**CONTRAINDICATIONS**

- **Respiratory System:** Has been removed from the labelling.

**WARNINGS**

**Important:** Do not administer intranasal DDAVP to patients who have had a previous allergic reaction to desmopressin acetate.

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DDAVP® Injection
desmopressin acetate
4 mcg/mL

DESCRIPTION
DDAVP® Injection (desmopressin acetate) 4 mcg/mL is a synthetic analogue of the natural pituitary hormone 8-arginine vasopressin (AVP), an antidiuretic hormone affecting renal water conservation. It is chemically defined as follows:

Empirical Formula: C₉H₁₄N₂O₆S⋅H₂O

DDAVP® Injection (desmopressin acetate) 4 mcg/mL is provided as a sterile, aqueous solution for injection. Each mL provides:

Desmopressin acetate 4 mcg
Sodium chloride 9 mcg
Hydrochloric acid to adjust pH to 4

The 10 mL vial contains chlorobutanol as a preservative (5 mg/mL).

CLINICAL PHARMACOLOGY

DDAVP Injection 4 mcg/mL contains as active substance, desmopressin acetate, a synthetic analogue of the natural hormone arginine vasopressin. One mL (4 mcg) of DDAVP (desmopressin acetate) solution has an antidiuretic activity of about 16 IU; 1 mcg of DDAVP is equivalent to 4 IU.

DDAVP has been shown to be more potent than arginine vasopressin in increasing plasma levels of factor VIII activity in patients with hemophilia and von Willebrand's disease type I.

Dose-response studies were performed in healthy persons, using doses of 0.1 to 0.4 mcg/kg body weight, infused over a 10-minute period. Maximal increases occurred at 0.3 to 0.4 mcg/kg. The response to DDAVP of factor VIII activity and plasminogen activator is dose-related, with maximal plasma levels of 300 to 400 percent of initial concentrations obtained after infusion of 0.4 mcg/kg body weight. The increase is rapid and evident within 30 minutes, reaching a maximum at a point ranging from 60 minutes to two hours. The factor VIII-related antigen and ristocetin cofactor activity were also increased to a smaller degree, but still are dose-dependent.

1. The biphasic half-lives of DDAVP were 7.8 and 75.5 minutes for the fast and slow phases, respectively, compared with 2.5 and 14.5 minutes for lysine vasopressin, another form of the hormone. As a result, DDAVP provides a prompt onset of antidiuretic action with a long duration after each administration.

2. The change in structure of arginine vasopressin to DDAVP has resulted in a decreased vasopressor action and decreased actions on visceral smooth muscle relative to the enhanced antidiuretic activity, so that clinically effective antidiuretic doses are usually below threshold levels for effects on central or visceral smooth muscle.

3. When administered by injection, DDAVP has an antidiuretic effect about ten times that of an equivalent dose administered intranasally.

4. The bioavailability of the subcutaneous route of administration was determined qualitatively using urine output data. The exact fraction of drug absorbed by that route to administration has not been quantitatively determined.

5. The percentage increase of factor VIII levels in patients with mild hemophilia A and von Willebrand's disease was not significantly different from that observed in normal healthy individuals when treated with 0.3 mcg/kg administered over 10 minutes.

6. Plasminogen activator activity increases rapidly after DDAVP infusion, but there has been no clinically significant fibrinolysis in patients treated with DDAVP.

7. The effect of repeated DDAVP administration when doses were given every 12 to 24 hours has generally shown a gradual diminution of the factor VIII activity increase noted with a single dose. The initial response is reproducible in any particular patient if there are 2 or 3 days between administrations.

Human Pharmacokinetics: DDAVP is mainly excreted in the urine. A pharmacokinetic study conducted in healthy volunteers and patients with mild, moderate, and severe renal impairment showed DDAVP to be eliminated primarily by renal excretion. No significant differences were observed between healthy persons and those with renal impairment.

DIABETES INSIPIDUS: DDAVP does not appear to alter the renal excretion of water, putting them at greater risk of hyponatremia. (See WARNINGS.)

CONTRAINDICATIONS

Von Willebrand's disease patients who are least likely to respond are those with severe homozygous von Willebrand's disease with factor VIII coagulant activity levels equal to or less than 5%.

DDAVP is contraindicated in 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 procedures.

DDAVP® Injection (desmopressin acetate) 4 mcg/mL is contraindicated in patients with episodes of spontaneous or trauma-induced injuries such as hemarthrosis, intracranial hematomas or mucosal bleeding.

DDAVP is not indicated for the treatment of hemophilia A with factor VIII coagulant activity levels equal to or less than 5%.

In certain clinical situations, it may be justified to try DDAVP® in patients with factor VIII levels between 2% and 5%; however, these patients should be carefully monitored.

CONTRAINDICATIONS

DDAVP Injection 4 mcg/mL is contraindicated for patients with mild to moderate classic von Willebrand's disease (Type I) with factor VIII levels greater than 5%. DDAVP will often maintain hemostasis in patients with mild to moderate von Willebrand's disease (Type I) who have factor VIII levels postoperatively when administered 30 minutes prior to surgical procedures. DDAVP® should not be used in patients with factor VIII levels between 2% and 5%.

DDAVP will often maintain hemostasis in patients with hemophilia A during surgical procedures and postoperatively when administered 30 minutes prior to scheduled procedures.

DDAVP® Injection is contraindicated in patients with episodes of spontaneous or trauma-induced injuries such as hemarthrosis, intracranial hematomas or mucosal bleeding.

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. (See WARNINGS.)

Diabetes Insipidus: DDAVP Injection 4 mcg/mL is indicated as antidiuretic replacement therapy in the management of central (cranial) diabetes insipidus and in the therapy of the ketogenic polyuria and polydipsia following head trauma or surgery in the pituitary region. DDAVP is ineffective for the treatment of nephrogenic diabetes insipidus.

Contraindications: DDAVP® should be used as an intranasal preparation. However, this means of delivery can be compromised by a variety of factors that can make nasal insufflation ineffective or inapplicable. These include poor intranasal absorption, nasal congestion and blockage, nasal discharge, atrophy of nasal mucosa, and severe atrophic rhinitis. Intranasal delivery may be inapplicable where there is an impaired level of consciousness. In addition, cranial surgical procedures, such as transsphenoidal hypophysectomy, create situations where an alternative route of administration must be used as in cases of nasal packing or recovery from surgery.

DDAVP® Injection 4 mcg/mL is contraindicated in individuals with known hypersensitivity to desmopressin acetate or to any of the components of DDAVP Injection 4 mcg/mL.

DDAVP® Injection is contraindicated in patients with moderate to severe renal impairment (defined as a creatinine clearance below 50 mL/min). DDAVP® is contraindicated in patients with hemophilia or a history of hyponatremia.

WARNINGS

Von Willebrand's disease patients who are least likely to respond are those with severe homozygous von Willebrand's disease with factor VIII coagulant activity levels less than 1%. Other patients may respond in a variable fashion depending on the type of molecular defect they have. Bleeding time and factor VIII coagulant activity, ristocetin cofactor activity, and von Willebrand factor antigen should be checked during administration of DDAVP to ensure that adequate levels are being achieved.

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. (See WARNINGS.)

Diabetes Insipidus: DDAVP Injection 4 mcg/mL is indicated as antidiuretic replacement therapy in the management of central (cranial) diabetes insipidus and in the therapy of the ketogenic polyuria and polydipsia following head trauma or surgery in the pituitary region. DDAVP is ineffective for the treatment of nephrogenic diabetes insipidus.

DDAVP® Injection is contraindicated in individuals with known hypersensitivity to desmopressin acetate or to any of the components of DDAVP®. DDAVP® is contraindicated in patients with moderate to severe renal impairment (defined as a creatinine clearance below 50 mL/min). DDAVP® is contraindicated in patients with hemophilia or a history of hyponatremia.

WARNINGS

1. Very rare cases of hyponatremia have been reported from world-wide postmarketing experience in patients treated with DDAVP® (desmopressin acetate) injection. In most cases, hyponatremia is not associated with an antidiuretic effect, in particular in pediatric and geriatric patients. Fluid intake should be adjusted downward to decrease the potential occurrence of water intoxication and hyponatremia. (See DRUG INTERACTIONS, Pediatric Use and Geriatric Use.) All patients receiving DDAVP therapy should be observed for the following signs or symptoms associated with hyponatremia: headache, nausea/vomiting, decreased serum sodium, weight gain, restlessness, fatigue, dehydrated appearance. Loss of appetite, thirst, diabetes, dehydration, physical or mental weakness, muscle spasm or cramps and abnormal mental status such as hallucinations, decreased consciousness and confusion. Severe symptoms may include one or a combination of the following: confusion, coma, convulsions. Particular attention should be paid to the possibility of the rare occurrence of an extreme decrease in plasma osmolality that may result in seizures which could lead to coma.

2. DDAVP should not be used to treat patients with Type IB von Willebrand's disease since platelet aggregation may be induced.

3. DDAVP should be used with caution in patients with habitual or psychogenic polydipsia who may be more likely to drink excessive amounts of water.
PRECAUTIONS

General: For injection only.

DDAVP Injection (desmopressin acetate) 4 mcg/mL has infrequently produced changes in blood pressure causing either a slight elevation in blood pressure or a transient fall in blood pressure and a compensatory increase in heart rate. The drug should be used with caution in patients with cardiac, coronary artery insufficiency and/or hypertension.

DDAVP (desmopressin acetate) should be used with caution in patients with conditions associated with fluid and electrolyte imbalance, such as cyclic fibrosis, heart failure and renal disorders, because these patients are prone to hyponatremia.

There have been rare reports of thrombotic events following DDAVP injection 4 mcg/mL, in patients predisposed to thrombus formation. No causality has been determined, however, the drug should be used with caution in these patients.

Severe allergic reactions have been reported. Anaphylaxis has been reported rarely with Intranasal and Intraosseous DDAVP. Including isolated case reports of intranasal bolus DDAVP to 150 mcg administered at intranasal doses of 4 mcg/mL, are produced by anaphylactic reaction or anaphylactic shock that may be facilitated by repeated injections.

Hemophilia A: Laboratory tests for assessing patient status include levels of factor VIII coagulant, factor VII antigen and factor VIII von Willebrand factor (von Willebrand factor) as well as factor VIII coagulant activity should be determined before giving any dose of DDAVP. If factor VII coagulant activity is present at less than 5% of normal, DDAVP should not be used.

von Willebrand's Disease: Laboratory tests for assessing patient status include levels of factor VIII coagulant activity, factor VII coagulant activity and factor VIII von Willebrand factor antigen. The skin bleeding time may be helpful in following these patients.

Diabetes Insipidus: Laboratory tests include urine volume and similarly. In some cases, plasma corosinly may be required.

Drug Interactions: Although the pressor activity of DDAVP is very low compared with the antidepressant activity, use of doses as large as 0.3 mcg/mL of DDAVP with other pressor agents should be done only with careful patient monitoring. This concomitant administration of drugs that may increase the risk of water intoxication with hyponatremia, (e.g., tricyclic antidepressants, selective serotonin re-uptake inhibitors, chlorpromazine, olaopine analogics, NSAMIDs, lamotrigine and carbamazepine) should be performed with caution.

DDAVP has been used with epalbuminamic acid without adverse effects.

Carcinogenicity, Mutagenicity, Impairment of Fertility: Studies with DDAVP have not been performed to evaluate carcinogenic potential, mutagenic potential or effects on fertility.

Pregnancy Category B: Fertility studies have not been done. Toxicology studies in rats and rabbits at doses from 0.05 to 10 mcg/kg/day (appraxonmately 0.1 times the maximum systemic human exposure in rats and up to 38 times the maximum systemic human exposure in rabbits based on surface area, mg/m2) revealed no harm to the fetus due to DDAVP. There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human responses, this drug should be used during pregnancy only if clearly indicated.

Several publications of desmopressin acetate use in the management of diabetes insipidus during pregnancy are available; these include a few anecdotal reports of congenital anomalies and low birth weight babies. However, no causal connection between these events and desmopressin acetate has been established. A fifteen year, Swedish, epidemiologic study of the use of DDAVP in pregnancy of age with diabetes insipidus found the rate of birth defects to be no greater than that in the general population; however, the statistical power of this study was limited.

Studies with DDAVP have not been performed to evaluate carcinogenic potential, mutagenic potential or effects on fertility. Studies with DDAVP have also not been performed to evaluate the potential for DDAVP to cause birth defects in human pregnancy.

There have been no controlled studies in nursing mothers. A single study in normal women demonstrated a marked change in plasma, but little if any change in assuable DDAVP in breast milk following an intranasal dose of 10 mcg. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when DDAVP is administered to a nursing woman.

Pediatric Use: Use in infants and pediatric patients will require careful fluid intake restriction to prevent possible hyponatremia and water intoxication. Use in infants and pediartic patients will require careful fluid intake restriction to prevent possible hyponatremia and water intoxication. Several studies of desmopressin acetate’s use in the management of diabetes insipidus during pregnancy are available; these include a few anecdotal reports of congenital anomalies and low birth weight babies. However, no causal connection between these events and desmopressin acetate has been established. A fifteen year, Swedish, epidemiologic study of the use of DDAVP in pregnancy of age with diabetes insipidus found the rate of birth defects to be no greater than that in the general population; however, the statistical power of this study was limited.

Geriatric Use: Clinical studies of DDAVP Injection did not include sufficient numbers of subjects aged 65 and over to determine whether the drug would respond differently from younger adults. In general, dose selection in elderly patients should be cautious, and it may be useful to monitor renal function. (See WARNINGS, PRECAUTIONS, Pediatric Use and Geriatric Use.)

DDAVP is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function. DDAVP is contraindicated in patients with renal insufficiency or with dehydration. (See CLINICAL PHARMACOLOGY, Human Pharmacokinetics and CONTRAINDICATIONS).

Use of DDAVP injection in geriatric patients will require careful fluid intake restrictions to prevent possible hyponatremia and water intoxication.

ADVERSE REACTIONS

Intranasal DDAVP has produced transient headache, nausea, mild abdominal cramps and vuvul pain. These symptoms disappeared with reduction in dosage. Occasionally, injection of DDAVP has produced local erythema, swelling or burning pain. Occasional flushing has been reported rarely with intranasal administration. (See CLINICAL PHARMACOLOGY, Human Pharmacokinetics and CONTRAINDICATIONS.) In case of overdosage, the dosage should be reduced, frequency of administration decreased, or the drug withdrawn according to the severity of the condition.

There is no known specific antidote for desmopressin acetate or DDAVP Injection 4 mcg/mL. An oral dose of 2 mcg/kg in mice produced no effect. Fluid restriction should be discussed with the patient. (See WARNINGS, PRECAUTIONS, Pediatric Use and Geriatric Use.)

DIAGNOSTIC USE

Hemophilia A and von Willebrand's Disease (Type I): DDAVP Injection 4 mcg/mL is administered as an intranasal infusion at a dose of 0.3 mcg/kg (4 mcg/mL) for adults, 0.6 mcg/kg (8 mcg/mL) for children, 0.1 mcg/kg (1.5 mcg/mL) for infants and neonates, or 0.3 mcg/kg (4 mcg/mL) for children weighing more than 10 kg, 50 mL of diluent is recommended; in children weighing 10 kg or less, 10 mL of diluent is recommended. Blood pressure and pulse should be monitored during infusion. If DDAVP Injection 4 mcg/mL is used preoperatively, it should be administered 30 minutes prior to the scheduled procedure.

The necessity for repeat administration of DDAVP or use of any blood products for hemostasis should be determined by laboratory response as assessed by the patient's ability to control bleeding. The tendency toward prolonged bleeding (lossening of response) with repeated administration given more frequently than every 48 hours should be considered in treating each patient.

Fluid restriction should be observed. (See WARNINGS, PRECAUTIONS, Pediatric Use and Geriatric Use.)

Diabetes Insipidus: This formulation is administered subcutaneously or by direct intravenous injection. DDAVP Injection 4 mcg/mL dosage must be determined for each patient and adjusted according to the pattern of response. Response should be estimated by two parameters: adequate duration of sleep and adequate, not excessive, water turnover.

The usual dosage range in adults is 0.5 mL (2.0 mcg) to 1 mL (4.0 mcg) daily, administered intravenously or subcutaneously, usually in two divided doses, morning and evening doses should be separated adjusted for an adequate diurnal rhythm of water turnover. For patients who have been controlled on intranasal DDAVP and who must be switched to the injection form, either because of poor intranasal absorption or because of the need for surgery, the comparable antidiuretic dose of the injection is about one-tenth the intranasal dose.

Fluid restriction should be observed. (See WARNINGS, PRECAUTIONS, Pediatric Use and Geriatric Use.)

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

Geriatric Use: This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function. (See CLINICAL PHARMACOLOGY, Human Pharmacokinetics and CONTRAINDICATIONS, Geriatric Use.)

Directions for use of One Point Cut (OPC) Ampules for DDAVP Injection:

1. Use aseptic technique to clean ampule. Gently tap the top of the ampule to assist the flow of the solution from the upper portion of the ampule to the lower portion of the ampule.

2. Locate the blue dot on the upper portion of the ampule. Below this dot is a small spot on the neck of the ampule. Hold the ampule with the blue dot facing away from you.

3. Cover the vial with an appropriate vial. Apply pressure to the top and bottom portions of the ampule to snap the ampule open gently away from you.

HOW SUPPLIED

DDAVP Injection (desmopressin acetate) 4 mcg/mL is available as a sterile solution in vials of ten 1 mL single dose ampules (NDC 5566-2200-0) and in 10 mL multiple-dose vials (NDC 5566-2200-20), each containing 4 mcg DDAVP per mL. Store refrigerated to 2°C to 8°C (36 to 46°F).

Keep out of the reach of children.

Manufactured by:
Ferring Pharmaceuticals Inc.
Parsons, NJ 07640 USA
Origin Sweden

1.1 US Patents 5,500,413; 5,596,078; 5,763,407
Rev 04/2015
0000000000
Each mL DDAVP® Rhinal Tube contains 0.1 mg desmopressin acetate, 5 mg chlorobutanol, 9 mg sodium chloride, hydrochloric acid to adjust pH.

Dosage and Administration:
See package insert for dosage information. Before use, carefully read accompanying instructions.

WARNING:
Keep out of reach of children.

Store refrigerated 2–8°C (36–46°F).

Mfd for: Ferring Pharmaceuticals Inc.
Parsippany, NJ 07054 USA
Origin Sweden

Reference ID: 3843605
Each mL DDAVP® Rhinal Tube contains 0.1 mg desmopressin acetate, 5 mg chlorobutanol, 9 mg sodium chloride, hydrochloric acid to adjust pH.

Dosage and Administration:
See package insert for dosage information. Before use, carefully read accompanying instructions.

WARNING: Keep out of reach of children.

Pharmacist: Detach Patient Instruction Guide from package insert and dispense with product.

Store refrigerated 2–8°C (36–46°F).

Mfd for: Ferring Pharmaceuticals Inc. Parsippany, NJ 07054 USA
Origin Sweden

www.ferring.com

2.5 mL Bottle

FOR INTRANASAL USE ONLY

NDC 55566-2400-0

Reference ID: 3843605
Each mL of DDAVP® Nasal Spray contains 0.1 mg desmopressin acetate, 0.2 mg benzalkonium chloride solution (50%), 1.7 mg citric acid monohydrate, 3 mg disodium phosphate dihydrate, and 7.5 mg sodium chloride.

Dosage and Administration: See package insert for dosage information.

WARNING: Keep out of reach of children.

Store upright at Controlled Room Temperature 20–25°C (68–77°F) [see USP].

Mfd for: Ferring Pharmaceuticals Inc., Parsippany, NJ 07054 USA

Origin Sweden

Exp. Date: 04/30/15

Batch: 5 mL Bottle (50 Doses) ONLY
DDAVP® Nasal Spray
desmopressin acetate
Each mL of DDAVP® Nasal Spray contains 0.1 mg desmopressin acetate, 0.2 mg benzalkonium chloride solution (50%), 1.7 mg citric acid monohydrate, 3 mg disodium phosphate dihydrate and 7.5 mg sodium chloride.

Dosage and Administration:
See package insert for dosage information. Before use, carefully read accompanying instructions.

WARNING:
Keep out of reach of children.

Pharmacist:
Detach Patient Instruction Guide from package insert and dispense with product.

Store upright at Controlled Room Temperature 20–25°C (68–77°F) [see USP].

Mfd for:
Ferring Pharmaceuticals Inc.
Parsippany, NJ 07054 USA
Origin Sweden
www.ferring.com

Reference ID: 3843605
DDAVP injection 10 ml Vial Label R11

04/27/15

Colors Used:

PMS Process Blue  Black

Reference ID: 3843605
DDAVP® Injection
desmopressin acetate

Each mL of DDAVP® Injection contains
4 mcg desmopressin acetate, 5 mg chlorobutanol, 9 mg sodium chloride,
hydrochloric acid to adjust pH to 4.

Dosage and Administration: See package insert for dosage information.


Mfd for:
Ferring Pharmaceuticals Inc.
Parsippany, NJ 07054 USA
Origin Sweden
U.S. Patents 5,500,413; 5,595,078;
5,763,407
www.ferring.com
XXXXXXXXXX

NDC 55566-2300-0

DDAVP® Injection
desmopressin acetate

For Intravenous and Subcutaneous Use Only

4 mcg/mL

10 mL Vial

For Intravenous and Subcutaneous Use Only

4 mcg/mL

10 mL Vial

Mfd for:
Ferring Pharmaceuticals Inc.
Parsippany, NJ 07054 USA
Origin Sweden
U.S. Patents 5,500,413; 5,595,078;
5,763,407
www.ferring.com
XXXXXXXXXX

Reference ID: 3843605
Directions for use of OPC* ampules for DDAVP Injection

1. Use aseptic technique to clean ampule. Gently tap the top of the ampule to assist the flow of the solution from the upper portion of the ampule to the lower portion.

2. Locate the blue dot on the upper portion of the ampule. Below this dot is a small score on the neck of the ampule. Hold the ampule with the blue dot facing away from you.

3. Cover the vial with an appropriate wipe. Apply pressure to the top and bottom portions of the ampule to snap the ampule open away from you.

*One Point Cut.
DDAVP Injection-1mL-1Count-Ampule-Label-R7.ai
04/27/15

Colors Used:
PMS Process Blue  White INK  Black

Reference ID: 3843605