HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Desmopressin Acetate Tablets safely and effectively. See full prescribing information for Desmopressin Acetate Tablets.

DESMOPRESSIN ACETATE tablets, for oral use
Initial U.S. Approval: 1978

----------INDICATIONS AND USAGE----------

Desmopressin Acetate Tablets are a vasopressin analog indicated in:

- patients as antidiuretic replacement therapy in the management of central diabetes insipidus (1.1)
- patients aged 6 years and older for the management of primary nocturnal enuresis (1.2)
- pediatric patients aged 3 years and older to evaluate the capacity of the kidneys to concentrate urine (Renal Concentration Capacity Test) (1.3)

Limitations of Use:

Desmopressin Acetate Tablets are not indicated for:

- Treatment of nephrogenic diabetes insipidus (1.4)
- Use in adults with secondary nocturia (1.4)
- Use as a diagnostic agent for the renal concentration capacity test in febrile patients (>38.0°C) due to the risk of inaccurate results (1.4)

----------DOSAGE AND ADMINISTRATION----------

- Central Diabetes Insipidus Dosage (2.1):
  - Individualize the dosage for each patient and adjust the dosage according to the diurnal pattern of response.
  - Recommended starting dose is 0.05 mg desmopressin acetate (half of the 0.1 mg Desmopressin Acetate Tablet) orally two times a day.
  - Titrate the daily dosage as needed. The usual dosage range is 0.1 mg daily to 1.2 mg daily orally divided into two or three daily doses.
  - Monitor response by measuring urine volume and osmolality. Monitoring measurements of plasma osmolality may also be useful.
- Primary Nocturnal Enuresis Dosage (2.2):
  - Limit fluid intake to a minimum from 1 hour before administration, until the next morning, or at least 8 hours after administration.
  - Individualize the dosage for each patient and adjust the dosage according to response.
  - The recommended starting dose is 0.2 mg orally daily at bedtime.
  - The dose may be titrated up to the maximum dose of 0.6 mg daily at bedtime. The desired response is typically achieved with dosages of 0.2 mg daily or 0.4 mg daily.
- Renal Concentration Capacity Test Dosage (2.3):
  - Administer 0.6 mg desmopressin acetate (three 0.2 mg Desmopressin Acetate Tablets) orally at bedtime after bladder emptying.
  - Discard any urine passed within one hour from drug administration. Take a sample of urine from the first voided specimen, at least one hour but not more than 12 hours after drug administration, to measure urine osmolality.
- See the Full Prescribing Information for recommendations for switching between desmopressin acetate formulations (2.4)

----------DOSAGE FORMS AND STRENGTHS----------

Desmopressin Acetate Tablets:

- 0.1 mg
- 0.2 mg

----------CONTRAINDICATIONS----------

- Known hypersensitivity to desmopressin acetate or to any of the components of Desmopressin Acetate Tablets (4, 6)
- Patients with renal impairment (creatinine clearance below 50 mL/min) (4, 8.6, 12.3)
- Hyponatremia or a history of hyponatremia (4, 5.1)

----------WARNINGS AND PRECAUTIONS ----------

Hyponatremia: Excessive fluid intake when urine output is limited by the antidiuretic effect of desmopressin may lead to water intoxication with hyponatremia. Cases of hyponatremia have been reported. Unless properly diagnosed and treated, hyponatremia can be fatal. Instruct patients about proper fluid restriction and monitor serum sodium as needed (2.1, 5.1)

----------ADVERSE REACTIONS----------

Adverse reactions that have been identified in patients administered Desmopressin Acetate Tablets are headache and hyponatremia (6)

To report SUSPECTED ADVERSE REACTIONS, contact Ferring Pharmaceuticals Inc. at 1-888-FERRING (1-888-337-7464) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- *Drugs that Increase Risk of Hyponatremia:* Require more frequent monitoring of serum sodium (7.1)
- *Other Vasoconstrictors:* Concomitant use may elevate blood pressure and require a reduction in Desmopressin Acetate Tablets dosage (7.2)

----------USE IN SPECIFIC POPULATIONS----------

- *Pediatric Use:* Use requires careful fluid intake restriction to prevent hyponatremia with water intoxication (5.1, 8.4)
- *Geriatric Use*: Carefully monitor renal function; restrict fluid intake to prevent hyponatremia with water intoxication (5.1, 8.5).

See 17 for PATIENT COUNSELING INFORMATION

Revised: 10/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

**Sections or subsections omitted from the full prescribing information are not listed.*

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Central Diabetes Insipidus

Desmopressin Acetate Tablets are indicated as antidiuretic replacement therapy in the management of central diabetes insipidus.

1.2 Primary Nocturnal Enuresis

Desmopressin Acetate Tablets are indicated in patients aged 6 years and older for the management of primary nocturnal enuresis.

1.3 Renal Concentration Capacity Test

Desmopressin Acetate Tablets are indicated in pediatric patients aged 3 years and older to evaluate the capacity of the kidneys to concentrate urine.

1.4 Limitations of Use:

Desmopressin Acetate Tablets are not indicated for:

- Treatment of nephrogenic diabetes insipidus
- Use in adults with secondary nocturia
- Use as a diagnostic agent for the renal concentration capacity test in febrile patients (>38.0°C) due to the risk of inaccurate results.

2 DOSAGE AND ADMINISTRATION

2.1 Central Diabetes Insipidus Recommended Dosage

- Instruct patients about appropriate fluid restriction during Desmopressin Acetate Tablet treatment *[see Warnings and Precautions (5.1)]*.
- Individualize the dosage of Desmopressin Acetate Tablets for each patient and adjust the dosage according to the diurnal pattern of response. Estimate patient response by: duration of sleep and water turnover.
- Recommended starting dose for patients is 0.05 mg desmopressin acetate (half of the 0.1 mg Desmopressin Acetate Tablet) orally two times a day.
- Titrate the daily dosage as needed to obtain an adequate antidiuretic response. The usual dosage range is 0.1 mg daily to 1.2 mg daily orally divided into two or three daily doses.
- Monitor response by measuring urine volume and osmolality. Monitoring measurements of plasma osmolality may also be useful.

2.2 Primary Nocturnal Enuresis Recommended Dosage

- Instruct patients about appropriate fluid restriction during Desmopressin Acetate Tablet treatment. Limit fluid intake to a minimum from 1 hour before administration, until the next morning, or at least 8 hours after administration *[see Warnings and Precautions (5.1)]*.
- Individualize the dosage of Desmopressin Acetate Tablets for each patient and adjust the dosage according to response.
- The recommended starting dose for patients aged 6 years and older is 0.2 mg orally daily at bedtime.
- Based upon clinical response, the dose may be titrated up to 0.4 mg daily and, if needed, to the maximum dose of 0.6 mg daily.

2.3 Renal Concentration Capacity Test Recommended Dosage

- Ensure the patient is afebrile prior to testing *[see Indications and Usage (1.4)]*
- Pediatric patients aged 3 years and older: administer 0.6 mg desmopressin acetate (three 0.2 mg Desmopressin Acetate Tablets) orally at bedtime after bladder emptying.
- Discard any urine passed within one hour from drug administration. Take a sample of urine from the first voided specimen, at least one hour but not more than 12 hours after drug administration, to measure urine osmolality.

2.4 Switching Between Desmopressin Acetate Formulations

- Begin Desmopressin Acetate Tablets for patients previously on intranasal desmopressin acetate:
    - 12 hours after the last intranasal dose for CDI patients
    - 24 hours after the last intranasal dose for PNE patients.
- Monitor patients closely during the initial dose titration period.

3 DOSAGE FORMS AND STRENGTHS

Desmopressin Acetate Tablets:

- 0.1 mg: White, oval, convex tablet, scored on one side, with engraving “0.1” on the other side
- 0.2 mg: White, round, convex tablet, scored on one side, with engraving “0.2” on the other side

4 CONTRAINDICATIONS

Desmopressin Acetate Tablets are contraindicated in individuals with:

- Known hypersensitivity to desmopressin acetate or to any of the components of Desmopressin Acetate Tablets *[see Adverse Reactions (6)]*.
- Renal impairment defined as estimated creatinine clearance (CL_{cr}) less than 50 mL/min) *[see Use in Specific Populations, Renal Impairment (8.6) and Clinical Pharmacology (12.3)]*.
- Hyponatremia or a history of hyponatremia *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hyponatremia

Excessive fluid intake when urine output is limited by the antidiuretic effect of desmopressin may lead to water intoxication with hyponatremia. Cases of hyponatremia have been reported from postmarketing experience in patients treated with desmopressin acetate. Unless properly diagnosed and treated, hyponatremia can be fatal.

All patients receiving Desmopressin Acetate Tablets should be observed for the following signs or symptoms associated with hyponatremia: headache, nausea/vomiting, decreased serum sodium, weight gain, restlessness, fatigue, lethargy, disorientation, depressed reflexes, loss of appetite, irritability, muscle weakness, muscle spasms or cramps and abnormal mental status such as hallucinations, decreased consciousness and confusion. Severe symptoms due to an extreme decrease in serum sodium and plasma osmolality may include one or a combination of the following: seizure, coma and/or respiratory arrest.

In order to decrease the risk of water intoxication with hyponatremia, fluid restriction is recommended. Careful fluid intake restriction is particularly important in pediatric and geriatric patients because these patients are at greater risk of developing hyponatremia [*see Use in Specific Populations, Pediatric Use (8.4) and Geriatric Use (8.5)*]. More frequent monitoring of serum sodium levels is recommended in the following patients: those with conditions associated with fluid and electrolyte imbalance, such as cystic fibrosis, heart failure, renal disorders, habitual or psychogenic polydipsia or those taking concomitant drugs that may cause hyponatremia *[see Drug Interactions (7.1)]*.

Suspend treatment with Desmopressin Acetate Tablets for patients with primary nocturnal enuresis during acute intercurrent illness characterized by fluid and/or electrolyte imbalance (e.g., systemic infections, fever, recurrent vomiting or diarrhea) or under conditions of extremely hot weather, vigorous exercise or other conditions associated with increased water intake.

6 ADVERSE REACTIONS

The following serious reactions are described below and elsewhere in the labeling:

- Hyponatremia *[see Warnings and Precautions (5.1)]*.

Adverse Reactions from Clinical Studies or Postmarketing Reports

The following additional adverse reactions have been identified during clinical studies or from postmarketing reports with use of desmopressin. Because some of these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or to establish a causal relationship to drug exposure.

Cardiac disorders: hypertension

Gastrointestinal disorders: nausea, vomiting, diarrhea, constipation, abdominal cramps

General disorders: headache, malaise, drug ineffective, edema, fatigue

Hepatobiliary disorders: transient increases in AST (1.5 times the upper limit of normal)

Immune system disorders: severe allergic reactions, anaphylaxis has occurred with other formulations of desmopressin

Metabolism and nutrition: dehydration, hyponatremia, water intoxication with hyponatremia

Nervous system disorders: hyponatremic convulsions, hyponatremic convulsions associated with concomitant use of the following medications: oxybutinin and imipramine [*see Drug Interactions (7.1)]*, asthenia, coma, disturbance in attention, psychomotor hyperactivity, dizziness, somnolence, depressed level of consciousness, falls.

Psychiatric disorders: confusional state, abnormal behavior, emotional disorder, depression, hallucination, insomnia

Renal and urinary disorders: Bladder and urethral symptoms, including urinary retention, urine flow decreased, dysuria

Skin and subcutaneous tissue disorders: rash, dermatitis allergic, sweating, flushing, urticaria

Respiratory, thoracic and mediastinal disorders: dyspnea, epistaxis

7 DRUG INTERACTIONS

7.1 Other Drugs that may Increase Risk of Hyponatremia

The concomitant administration of Desmopressin Acetate Tablets with other drugs that may increase the risk of water intoxication with hyponatremia, (e.g., tricyclic antidepressants, selective serotonin re-uptake inhibitors, chlorpromazine, opiate analgesics, NSAIDs, lamotrigene and carbamazepine) requires more frequent serum sodium monitoring [*see Warnings and Precautions (5.1), Adverse Events (6)*].

7.2 Other Vasoconstrictors

Desmopressin acetate can elevate blood pressure. Use of large doses of Desmopressin Acetate Tablets with other vasoconstrictors may require a reduction of the Desmopressin Acetate Tablet dosage *[see Adverse Reactions (6)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk summary

Prolonged experience with desmopressin in pregnant women over several decades, based on the available published data and case reports, did not identify a drug associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. In addition, *in vitro* studies with human placenta demonstrate poor placental transfer of desmopressin. No adverse developmental outcomes were observed in animal reproduction studies with administration of desmopressin during organogenesis to pregnant rats and rabbits at doses approximately <1 and 38 times, respectively, the maximum recommended human dose based on body surface area (mg/m^2) (*see Data*).

The estimated background risk of major birth defects and miscarriage for the indicated population are unknown. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

Desmopressin acetate at up to 50 ng/kg/day was given by subcutaneous injection to pregnant rats, from gestation day 1 to 20 during the period of early embryonic development and organogenesis without teratogenic effects. Desmopressin acetate at up to 10 mcg/kg/day was given to pregnant rabbits by subcutaneous injection from gestation day 6 to 18 during fetal organogenesis without teratogenic effects. These doses of desmopressin acetate represent approximately <1 times (rat) and 38 times (rabbit) the maximum recommended human dose based on body surface area (mg/m^2).

8.2 Lactation

Risk Summary

Breastfeeding is not expected to result in clinically relevant exposure of the infant to desmopressin following maternal administration. Desmopressin is present in small amounts in human milk (*see Data*). There is no information on the effects of desmopressin on the breastfed infant or on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's need for Desmopressin Acetate Tablets and any potential adverse effects on the breastfed child from Desmopressin Acetate Tablets or from the underlying maternal condition.

Data

Human Data

The breast milk of lactating women was collected over 8 hours following desmopressin (300 mcg) administration using nasal spray. Based on the measured concentrations of desmopressin, the amounts of desmopressin that may be transferred to a breastfed infant correspond to 0.0001-0.005% of the dose administered.

8.4 Pediatric Use

Central Diabetes Insipidus

Desmopressin Acetate Tablets are indicated as antidiuretic replacement therapy in the management of central diabetes insipidus in pediatric patients. Use of Desmopressin Acetate Tablets for this indication is supported by evidence from adults and pediatric patients with central diabetes insipidus. Use in pediatric patients requires careful fluid intake restriction to prevent possible water intoxication with hyponatremia *[see Warnings and Precautions (5.1)]*.

Primary Nocturnal Enuresis

Desmopressin Acetate Tablets are indicated for the management of primary nocturnal enuresis in pediatric patients 6 years of age and older. Use of Desmopressin Acetate Tablets for this indication is supported by evidence from clinical trials in pediatric and adult patients with primary nocturnal enuresis. Temporarily suspend treatment with Desmopressin Acetate Tablets during acute intercurrent illness characterized by fluid and/or electrolyte imbalance (e.g., systemic infections, fever, recurrent vomiting or diarrhea) or under conditions of extremely hot weather, vigorous exercise or other conditions associated with increased water intake *[see Warnings and Precautions (5.1)]*.

Desmopressin Acetate Tablets are not indicated in pediatric patients less than 6 years of age.

Renal Concentration Capacity Test

Desmopressin Acetate Tablets are indicated to evaluate the capacity of the kidneys to concentrate urine in pediatric patients aged 3 years and older. Use of Desmopressin Acetate Tablets for this indication is supported by evidence from a clinical trial in pediatric patients.

Desmopressin Acetate Tablets are not indicated in pediatric patients less than 3 years of age.

8.5 Geriatric Use

Clinical studies of Desmopressin Acetate Tablets in the elderly have shown an increased risk of hyponatremia with age and declining creatinine clearance.

Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection and monitoring renal function is recommended [*see Section Clinical Pharmacology (12), Contraindications (4)*].

Use of Desmopressin Acetate Tablets in geriatric patients requires careful fluid intake restriction to prevent possible water intoxication with hyponatremia [*see Warnings and Precautions (5.1)*].

8.6 Renal Impairment

Desmopressin acetate is substantially excreted by the kidney, and the risk of adverse events may be greater in patients with renal impairment than patients with normal renal function. Desmopressin Acetate Tablets are contraindicated in patients with estimated CL_{cr} by Cockcroft-Gault equation less than 50 mL/min [*see Clinical Pharmacology (12.1, 12.3), Contraindications (4)*].

10 OVERDOSAGE

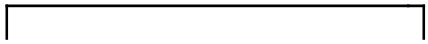
Signs of overdose may include confusion, drowsiness, continuing headache, problems with passing urine and rapid weight gain due to fluid retention. *[see Warnings and Precautions (5.1)]*. In case of overdosage, reduce the dosage, decrease the frequency of administration, or discontinue Desmopressin Acetate Tablets. There is no known specific antidote for desmopressin acetate.

11 DESCRIPTION

Desmopressin Acetate Tablets contain desmopressin acetate, a synthetic vasopressin analog, an antidiuretic hormone affecting renal water conservation. It is chemically defined as follows:

Mol. wt. 1183.34

Empirical formula: $C_{46}H_{64}N_{14}O_{12}S_2 \bullet C_2H_4O_2 \bullet 3H_2O$



SCH_2CH_2CO-Tyr-Phe-Gln-Asn-Cys-Pro-D-Arg-Gly-$NH_2 \bullet CH_3COOH \bullet 3H_2O$

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

Desmopressin acetate tablets contain either 0.1 or 0.2 mg desmopressin acetate which is equivalent to 0.089 mg desmopressin and 0.178 mg of desmopressin, respectively. Inactive ingredients include: lactose, potato starch, magnesium stearate and povidone.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The antidiuretic effects of desmopressin are mediated by stimulation of vasopressin 2 (V2) receptors, thereby increasing water re-absorption in the kidney, and hence reducing urine production. Desmopressin is a replacement hormone for antidiuretic hormone in the treatment of central diabetes insipidus.

12.2 Pharmacodynamics

The use of desmopressin in patients with central diabetes insipidus reduces urinary output, increases urine osmolality, and decreases plasma osmolality. Dose response studies in patients with diabetes insipidus have demonstrated that oral doses of 0.025 mg to 0.4 mg produced clinically significant antidiuretic effects. In most patients, doses of 0.1 mg to 0.2 mg produced optimal antidiuretic effects lasting up to eight hours. With doses of 0.4 mg, antidiuretic effects

were observed for up to 12 hours; measurements beyond 12 hours were not recorded. Following administration of desmopressin acetate tablets, the onset of antidiuretic effect occurs at around 1 hour, and it reaches a maximum at about 4 to 7 hours based on the measurement of increased urine osmolality.

12.3 Pharmacokinetics

Absorption

The mean time to reach maximum plasma desmopressin levels (t_{max}) is approximately 1.1 hours following Desmopressin Acetate Tablet administration. Increasing oral doses produced dose dependent increases in the plasma levels of desmopressin. The bioavailability of desmopressin acetate oral tablets is about 5% compared to intranasal formulation, and about 0.16% compared to intravenous formulation.

Distribution

The volume of distribution of desmopressin after intravenous administration of 2 mcg is 26.5 L.

Elimination

The mean terminal half-life after IV dosing of desmopressin is 2.8 hours.

Metabolism

In vitro studies in human liver microsome preparations have shown that desmopressin is not a substrate for the human CYP450 system.

Excretion

Desmopressin is mainly excreted in the urine. After intravenous administration of 2 mcg, 52% of the dose was recovered in the urine within 24 hours as unchanged desmopressin.

Specific Populations

Renal Impairment

Desmopressin is mainly excreted in the urine. A pharmacokinetic study was conducted in subjects with normal kidney function as well as mild, moderate, and severe renal impairment (n=24, 6 subjects in each group) with a single 2 mcg dose of desmopressin acetate injection. The terminal half-life was 2.8 hours in subjects with normal renal function, 4.0 hours in mild renal impairment, 6.6 hours in moderate renal impairment and 8.7 hours in severe renal impairment. In patients with mild, moderate and severe renal impairment, mean desmopressin exposure was 1.5 fold, 2.4 fold and 3.6 fold higher, respectively, compared to that of subjects with normal renal function *[see Contraindications (4), Use in Specific Populations (8.6)]*.

Drug Interactions

In vitro studies in human liver microsome preparations have shown that desmopressin does not inhibit the human CYP450 system. No *in vivo* interaction studies have been performed with Desmopressin Acetate Tablet.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies with desmopressin acetate have not been performed to evaluate carcinogenic potential, mutagenic potential or effects on fertility.

14 CLINICAL STUDIES

Central Diabetes Insipidus

Clinical studies were conducted [*see Clinical Pharmacology (12.2*)].

Primary Nocturnal Enuresis in Pediatric Patients

Two double-blind, randomized, placebo-controlled studies were conducted in a total of 329 patients with primary nocturnal enuresis with data available for efficacy. Patients were 5-17 years old, and 72% were males. Patients were evaluated over a two-week baseline period in which the average number of wet nights was 10 (range 4-14). Patients were then randomized to receive 0.2, 0.4, or 0.6 mg of desmopressin acetate or placebo. The pooled results after two weeks are shown in Table 1:

Table 1. Response to Desmopressin Acetate Tablets and Placebo at Two Weeks of Treatment Mean (SE) Number of Wet Nights/2 Weeks

	Placebo (n = 85)	**0.2 mg/day (n = 79)**	**0.4 mg/day (n = 82)**	**0.6 mg/day (n = 83)**
Baseline	10 (0.3)	11 (0.3)	10 (0.3)	10 (0.3)
Reduction from Baseline	1 (0.3)	3 (0.4)	3 (0.4)	4 (0.4)
Percent Reduction from Baseline	10%	27%	30%	40%
p-value vs placebo	——	<0.05	<0.05	<0.05

Patients treated with Desmopressin Acetate Tablets showed a statistically significant reduction in the number of wet nights compared to placebo-treated patients. A greater response was observed with increasing doses up to 0.6 mg.

Primary Nocturnal Enuresis in Pediatric Patients Aged 12 and Older and Adults

A double-blind, randomized, parallel-group study was conducted in 66 patients with primary nocturnal enuresis who were determined to be responders to therapy with Desmopressin Acetate Nasal Spray (e.g., >50% reduction in the number of wet nights/week) and continued to have at least one wet night per week during the washout period. The median age of the subjects was 17 with a range of 12 to 45 years, 56% were males, and they had an average of 5 wet nights per week (range 2-7) at baseline. Patients were randomized to receive 0.2 or 0.4 mg of Desmopressin Acetate Tablets. Treatment outcome was measured as a mean reduction in the number of wet

nights per week at the end of the four week treatment period relative to the baseline observation period. The results by age group are shown in Table 2:

Table 2. Response to Desmopressin Acetate Tablets at Four Weeks of Treatment Mean (SD) Number of Wet Nights/Week

Age	12-17 years of age		18-45 years of age	
	0.2 mg/day (n = 13)	**0.4 mg/day (n = 17)**	**0.2 mg/day (n = 18)**	**0.4 mg/day (n = 15)**
Baseline	5.5 (1.0)	4.5 (1.4)	5.7 (1.1)	4.7 (1.4)
Reduction from Baseline*	1.7 (0.5)	3.6 (0.4)	3.7 (0.4)	3.8 (0.4)
Percent Reduction from Baseline	31%	80%	65%	81%

*Least square mean (SE) adjusted for baseline

Renal Concentration Capacity Test in Pediatric Patients

A multi-center, randomized, double-blind, double-dummy, four-period, cross-over trial was performed in 153 patients aged 3 to 18 years to compare Desmopressin Acetate Tablets (0.6 mg), Desmopressin Acetate Nasal Spray (20 mcg) and placebo. Patients were given medication in the evening before bedtime, with fluid restriction maintained from one hour before dosing to 8 hours after dosing. Any urine sample within one hour of drug administration was discarded. Urine osmolality was measured in the first voided specimen, at least one hour but not more than 12 hours after drug administration. The results of the test are shown in Table 3:

Table 3. Urine Osmolality (mOsm/kg) in Pediatric Patients Treated with Desmopressin Acetate Tablets, Nasal Spray and Placebo (ITT population)

	Tablet 0.6 mg (3×0.2 mg)	**Nasal Spray 20 µg (2×10µg)**	**Placebo**
N	137	144	141
Mean (SD)	930 (149)	962 (187)	718 (238)
Tablet vs. Nasal Spray	-41 (-62, -19)		
LSMean difference (95% Cl)			

16 HOW SUPPLIED/STORAGE AND HANDLING

Desmopressin Acetate Tablets are available as:

- 0.1 mg tablet: White, oval, convex tablet, scored on one side, with engraving “0.1” on the other side
  NDC 55566-5060-1, Bottle of 100 tablets

- 0.2 mg tablet: White, round, convex tablet, scored on one side, with engraving “0.2” on the other side
  NDC 55566-5061-1, Bottle of 100 tablets

Store at Controlled Room Temperature 20 to 25°C (68 to 77°F) [see USP]. Avoid exposure to excessive heat or light.

17 PATIENT COUNSELING INFORMATION

Hyponatremia and Fluid Restriction

- Inform patients that Desmopressin Acetate Tablets may cause severe hyponatremia, which may be life-threatening, if it is not promptly diagnosed and treated. Inform patients about the signs and symptoms associated with hyponatremia and advise them to contact a healthcare provider if these occur [*see Warnings and Precautions (5.1)*].
- Advise patients to limit fluid intake to a minimum starting one hour prior to Desmopressin Acetate Tablet administration and for eight hours following Desmopressin Acetate Tablet administration. [*see Warnings and Precautions (5.1)*].

U.S. Patent Nos. 5,500,413, 5,596,078, 5,674,850, 5,047,398; 5,763,407

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

FERRING
PHARMACEUTICALS