

# Desmopressin PH&T

Desmopressin Acetate, 0.1mg/ml, nasal spray

## Presentation

DESMOPRESSIN PH&T 0.1mg/ml nasal spray solution. 1ml nasal spray solution contains 0.1mg desmopressin acetate equivalent to desmopressin 0.089mg.

A clear, colorless solution in a glass bottle

## Uses

### *Actions*

Pharmacotherapeutic group: vasopressin and analogues. ATC code: H01B A02.

DESMOPRESSIN PH&T nasal spray solution contains desmopressin, a structural analogue of the natural pituitary hormone arginine vasopressin. The difference lies in the dissemination of cysteine and substitution of L-arginine by D-arginine. This results in a considerably longer duration of action and a complete lack of pressor effect in the dosages clinically used.

### *Pharmacokinetics*

The bioavailability is about 3-5%. Maximum plasma concentration is reached after approximately one hour. An intranasal dose of 10-20µg provides an antidiuretic effect during 8-12 hours. Desmopressin is excreted mainly in the urine.

### *Indications*

DESMOPRESSIN PH&T nasal spray solution is indicated for the treatment of cranial diabetes insipidus and for establishing renal concentration capacity testing.

DESMOPRESSIN PH&T nasal spray solution is also indicated for the treatment of primary nocturnal enuresis in patients (from 5 years of age) with normal ability to concentrate urine.

## Dosage and Administration

1 dose of the spray provides 0.1ml, which corresponds to 10µg desmopressin acetate.

### *Cranial diabetes insipidus*

Dosage is individual after testing, but normal dosage for adults is 10-20µg 1-2 times daily. For children 5-10µg 1-2 times daily

In the event of signs of water retention/hyponatremia treatment should be interrupted and the dose should be adjusted.

### ***Primary nocturnal enuresis***

A clinically effective dose is individual and may vary from 10 to 40µg administered intranasally. A suitable initial dose is 20µg intranasally at bedtime. Fluid restriction should be observed, please see under Warnings and Precautions. In the event of signs of water retention/hyponatremia treatment should be interrupted. Assessment of the necessity of continued treatment should be made after three months during one substance-free week.

### ***Renal function testing***

To establish renal concentration capacity, the following single doses are recommended:

The normal dose for adults is 40µg.

For children over 1 year 20µg

For children under 1 year 10µg

After administration of DESMOPRESSIN PH&T nasal spray solution any urine collected within one hour is discarded. During the next 8 hours 2 portions of urine are collected for osmolality testing. Fluid restriction should be observed, see under Warnings and Precautions.

## **Contraindications**

DESMOPRESSIN PH&T nasal spray solution is contraindicated in cases of:

- habitual or psychogenic polydipsia
- cardiac insufficiency and other conditions requiring treatment with diuretics
- hypersensitivity to desmopressin or any of the excipients

## **Warnings and Precautions**

Only use nasal spray in patients where orally administered formulations are not feasible (see Post-Marketing Experience).

DESMOPRESSIN PH&T nasal spray solution should be used with caution in:

- Very young and elderly patients
- Conditions characterised by fluid and/or electrolyte imbalance
- Patients at risk for increased intracranial pressure

Renal concentration capacity testing in children below the age of 1 year should only be performed in hospital and under careful supervision. When used for diagnostic purposes the fluid intake must be limited to a maximum of 0.5 litres to quench thirst from 1 hour before until 8 hours after administration.

When used for enuresis the fluid intake must be limited to a minimum from 1 hour before until 8 hours after administration.

## ***Use in pregnancy and lactation***

### **Pregnancy**

Reproduction studies performed in rats and rabbits with doses more than 100 times the human dose have revealed no evidence of a harmful action of desmopressin on the foetus. One investigator has reported 3 cases of malformations in children to mothers suffering from diabetes insipidus and receiving desmopressin during pregnancy. However, several other published reports comprising more than 120 cases show that women treated with desmopressin during pregnancy have given birth to normal children. Furthermore a review of a very large data set identifying 29 children who have been exposed to desmopressin during the full pregnancy shows no increase in the malformation rate in the children born.

### **Lactation**

Results from analyses of milk from nursing mothers receiving high dose desmopressin (300µg intranasal), indicate that the amounts of desmopressin that may be transferred to the child are considerably less than the amounts required to influence diuresis.

## ***Effects on ability to drive and use machines***

None

## **Adverse Effects**

### ***Common (>1/100)***

#### **General**

Headache

#### **GI**

Stomach pain, nausea

#### **Upper respiratory**

Nasal congestion/rhinitis, epistaxis.

Treatment without concomitant reduction of fluid intake may lead to water retention/hyponatremia with accompanying signs and symptoms (headache, nausea/vomiting, decreased serum sodium, weight gain, and in serious cases, convulsions).

Post marketing experience:

Very rare cases of emotional disturbances in children have been reported.

Isolated cases of allergic skin reactions and more severe general allergic reactions have been reported.

Hyponatraemia is an infrequent but serious adverse event which has been reported at a rate of approximately 15 cases per 100,000 patient years of exposure for intranasal solutions and 6 cases per 100,000 patient years for oral formulations.

## **Interactions**

Substances, which are known to release antidiuretic hormone, e.g. tricyclic antidepressants, chlorpromazine and carbamazepine, may cause an additive antidiuretic effect leading to an increased risk of water retention/hyponatremia.

Indomethacin increases the urine concentrating effect of desmopressin without influencing the duration. The effect is probably without any clinical significance.

## **Overdosage**

Overdose of desmopressin nasal spray solution can lead to water retention with hyponatremia.

### ***Treatment***

Although the treatment of hyponatremia should be individualised, the following general recommendations can be given. Asymptomatic hyponatremia is treated by discontinuing the desmopressin treatment and fluid restriction. Infusion of isotonic or hypertonic sodium chloride may be added in cases with symptoms. When the water retention is severe (convulsions and unconsciousness) treatment with furosemide should be added.

## **Pharmaceutical Precautions**

### ***List of excipients***

Sodium chloride, hydrochloric acid (for pH adjustment), chlorobutanol hemihydrate (preservative) and purified water.

### ***Incompatibilities***

Not applicable

### ***Shelf-life***

DESMOPRESSIN PH&T nasal spray is stable for two years when stored unopened at 2 – 8°C. After opening, discard after 2 months. DESMOPRESSIN PH&T can be stored at 25°C for two months.

### ***Special precautions for storage***

DESMOPRESSIN PH&T nasal spray solution should be stored at in an upright position at 2 – 8°C, in the original package. After opening, discard after 2 months.

DESMOPRESSIN PH&T nasal spray can also be stored at 25°C for two months.

### ***Instructions for use/handling***

Before DESMOPRESSIN PH&T nasal spray solution is used for the first time, prime the pump by pressing downward 4 or 5 times or until an even spray is obtained. If the spray has not been used for a week it is necessary to prime the pump again by pressing it downwards once or until an even spray is obtained.

At administration it is important that the end of the tube inside the bottle is submerged in the liquid. The head is to be tipped slightly back while inserting the applicator straight into the nostril. Instructions for use are enclosed with the package.

The spray bottle should always be stored in an upright position with the protective cap in place.

## **Medicine Classification**

Prescription Medicine

## **Package Quantities**

Amber glass vial (Ph Eur Type 1).

Vial fill-volume: 6ml (60 doses)

DESMOPRESSIN PH&T nasal spray is actuated by a manual dose pump without propellant. The spray pump is designed to deliver 100µl solution (= 10µg desmopressin acetate) per dose.

## **Further Information**

### ***Pre-clinical safety data***

There were no unusual findings during the examination of the safety and safety profile of desmopressin.

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