

ADIN NASAL SPRAY

Desmopressin acetate

Presentation

ADIN 0.1mg/ml nasal spray solution. 1ml nasal spray solution contains 0.1mg desmopressin acetate equivalent to desmopressin 0.089mg. A clear, colourless solution in an amber glass bottle.

Uses

Actions

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

ADIN nasal spray solution contains desmopressin, a structural analogue of the natural pituitary hormone arginine vasopressin. The difference lies in the desamination 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

ADIN nasal spray solution is indicated for the treatment of central diabetes insipidus and for establishing renal concentration capacity testing.

ADIN 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.

Central 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 dose is 20µg intranasally at bedtime. Start at lowest dose. Increase progressively and with caution. Fluid restriction should be observed, (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 ADIN 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

ADIN nasal spray solution is contraindicated in cases of:

- habitual or psychogenic polydipsia (resulting in a urine production exceeding 40mL/kg/24 hours)
- syndrome of inappropriate ADH secretion (SIADH)
- known hyponatraemia
- history of known or suspected cardiac insufficiency and other conditions requiring treatment with diuretics
- moderate and severe renal insufficiency (creatinine clearance below 50mL/min)
- hypersensitivity to desmopressin or to any of the excipients

Warnings and Precautions

Only use nasal spray in patients where orally administered formulations are not feasible.

ADIN 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.

Ensure that in children administration is under adult supervision.

Severe bladder dysfunction and outlet obstruction should be considered before starting treatment for primary nocturnal enuresis.

Precautions

Severe bladder dysfunction and outlet obstruction should be considered before starting treatment for primary nocturnal enuresis.

Precautions to avoid hyponatraemia, including careful attention to fluid restriction and more frequent monitoring of serum sodium, must be taken in case of concomitant treatment with medicines, which are suspected to induce SIADH, e.g. tricyclic antidepressants, selective serotonin reuptake inhibitors, chlorpromazine and carbamazepine and in case of concomitant treatment with NSAID.

Treatment with desmopressin should be interrupted during acute intercurrent illness characterised by fluid and/or electrolyte imbalance (such as systemic infections, fever, gastroenteritis).

Use in pregnancy and lactation

Pregnancy

Published data on a limited number (n = 53) of exposed pregnancies in women with diabetes insipidus indicate no adverse effects of desmopressin on pregnancy or on the health of the foetus/newborn child. To date, no other relevant epidemiological data are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Caution should be exercised when prescribing to pregnant women.

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.

Post marketing experience

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 years for oral formulations.

Interactions

Substances, which are known to induce SIADH, e.g. tricyclic antidepressants, selective serotonin reuptake inhibitors, 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.

NSAIDs may induce fluid retention/hyponatraemia.

Overdosage

Overdose of ADIN 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, Citric Acid monohydrate, Disodium Phosphate dihydrate, Benzalkonium Chloride, Purified Water.

Incompatibilities

Not applicable.

Shelf-life

ADIN nasal spray is stable for three years when stored unopened at room temperature (max 25°C). After opening, discard after 2 months.

Special precautions for storage

ADIN nasal spray solution should be stored at room temperature (up to 25°C).

Instructions for use/handling

Before ADIN nasal spray solution is used for the first time, prime the pump by pressing downward 4 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.

Medicine Classification

Prescription Medicine.

Package Quantities

Brown Type I glass vial. Fill-volume: 5ml, 6ml.

ADIN 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.

Name and Address

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