

MINIRIN NASAL DROPS

Desmopressin acetate

Presentation

MINIRIN 0.1mg/ml nasal drops solution contains 0.1mg desmopressin acetate which corresponds to 0.089mg desmopressin per mL. A clear, colourless solution in an amber glass bottle.

Uses

Actions

Pharmacotherapeutic group: Vasopressin and analogues, ATC code: H01B A02.

MINIRIN nasal drops 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

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

MINIRIN nasal drops 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

One mark of the rhinyle tube (0.05ml) corresponds to 5µg 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 dose progressively and with caution. 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 MINIRIN nasal drops 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

MINIRIN nasal drops are contraindicated in cases of:

- habitual or psychogenic polydipsia (resulting in a urine production exceeding 40 mL/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 50 mL/min)
- hypersensitivity to desmopressin or to any of the excipients

Warnings and Precautions

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

MINIRIN nasal drops 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

For renal concentration capacity testing

Renal concentration capacity testing in children below the age of 1 year should only be performed in hospital and under careful supervision. 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.

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 a high dose of desmopressin (300µg intranasally), 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:

- Isolated 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 formulations 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 MINIRIN nasal drops solution can lead to water retention and 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

Chlorobutanol hemihydrate, Sodium Chloride, Hydrochloric Acid, Purified Water.

Incompatibilities

Not applicable.

Shelf-life

3 years.

Special precautions for storage

MINIRIN nasal drops solution should be stored at 2°C-8°C.

Instructions for use/handling

The preparation is to be administered according to the instructions for use supplied with the package.

Medicine Classification

Prescription Medicine.

Package Quantities

Nature and contents of container

Brown Type I glass vial, fitted with a dropper set + 2 rhinyle tubes (volume marks are indicated on the rhinyle tube from 0.025 to 0.20ml printed in black).

Pack sizes

2.5ml.

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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11 September 2007

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