Minirin®

Nasal spray 10 microg/dose

FERRING

Declaration
Each ml of solution contains desmopressin acetate 0.1 mg, benzalkonium chloride (preservative) constituents and purified water to 1 ml.

Presentation
MINIRIN nasal spray is supplied in bottles provided with precompression spray pumps designed to deliver 10 micrograms per actuation.

Properties
MINIRIN contains desmopressin, a structural analogue of the natural hormone arginine vasopressin. Two chemical changes have been made to the natural hormone, namely desamination of 1-cysteine and substitution of 8-L-arginine by 8-D-arginine.These structural changes result in a compound with significantly increased antidiuretic potency, very little activity on smooth muscle, hence the avoidance of undesirable pressor side effects, intranasal administration of 10-20 µg desmopressin provides an antidiuretic effect, lasting in most patients for 8-12 hours.

Indications
Central diabetes insipidus
The use of MINIRIN in patients with an established diagnosis will result in a reduction in urinary output with concomitant increase in urine osmolality and decrease in plasma osmolality. This will result in decreased urinary frequency and decreased nocturia.
Renal concentrating capacity test
MINIRIN can be used to test the capacity of the kidneys to concentrate urine; as a diagnostic aid in the examination of the kidney function. This is especially useful in the differential diagnosis between levels of urinary tract infections.
Cystitis will opposite to pyelonephritis not cause a subnormal ability to concentrate urine.

Contraindications
MINIRIN must not be used in cases of:
- habitual and psychogenic polydipsia
- cardiac insufficiency and other conditions requiring treatment with diuretic agents
- syndrome of inappropriate ADH secretion (SIADH)
- known hyponatraemia
- moderate to severe renal impairment (creatinine clearance less than 50 ml/min)
- hypersensitivity to desmopressin or to any of the excipients.

Special precautions for use
Precautions to prevent fluid overload must be taken in:
- the very young and elderly patients
- conditions characterized by fluid and/or electrolyte imbalance
- patients at risk for increased intracranial pressure

Additional precaution for using the renal concentrating capacity test:
-Renal concentrating capacity testing in children below the age of 1 year should only be performed under carefully supervised conditions in hospital.

Pregnancy
Reproduction studies performed on 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 compromising 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 (30 µg intranasally), indicate that the amounts of desmopressin that may be transferred to the child are considerably less than the amounts required to influence diuresis.

Undesirable effects
A few percent of treated patients can be expected to experience side effects such as headache, nausea and stomach pain.

Common (> 1/100)	*General*: Headache *GI*: Stomach pain, nausea *Upper respiratory*: Nasal congestion/rhinitis, epistaxis
Less common (1/100-1/1000)	*Skin*: Allergic reactions to the preservative

Treatment without concomitant restriction of water intake may lead to water retention with accompanying signs and symptoms (reduced serum sodium, weight gain, and, in serious cases, convulsions).

Interactions
Substances that are known to induce disturbed ADH secretion, e.g. tricyclic antidepressants, SSRIs, chloropromazine and carbamazepine may cause an additive antidiuretic effect with an increased risk of fluid retention.
NSAID preparations can induce water retention/hyponatraemia.

Dosage and administration
Central diabetes insipidus: Dosage is individual but clinical experience has shown that the average daily dose in adults is 20 µg to 40 µg and for children 10µg to 20µg. This may be given as a single dose or divided into two or three doses. About one third of patients can be treated with a single daily dose.

If signs of water retention/hyponatraemia develop, treatment should be temporarily discontinued and the dose adjusted. Fluid intake should be restricted. If signs of water retention and/or hyponatraemia develop (headache, nausea/vomiting, weight gain and in serious cases convulsions), treatment should be discontinued until the patient has recovered. Fluid intake should be strictly limited when treatment is reinstated.

Renal concentrating capacity test: Normal adult dose is 40 µg. for children over 12 months the dose is 10-20 µg. for children under 12 months the dose is 10 µg. After administration of MINIRIN possible urine within 1 hour is discarded. During the next 8 hours 2 portions of urine are collected for measurement of urine osmolality. A restricted water intake must be observed, see also under special warnings.

The reference level for normal urine osmolality after MINIRIN administration is 800 mOsm/kg for most patients. With values under this level, the test should be repeated. A similar low result indicates an impaired ability to concentrate urine and the patient should be referred for further examination into the underlying cause of the malfunction.

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

Special warnings
When used for diagnostic purpose the fluid intake must be limited and not exceed 0.5L from 1 hour before until 8 hours after administration.
Substances which are known to release antidiuretic hormone, eg. Tricyclic antidepressants, chlorpromazine and carbamazepine, may cause an additive antidiuretic effect and increase the risk of water retention.

Recommendations when Minirin is prescribed:
- administration to children should be supervised by an adult to ensure the correct dose is given.

If there is no simultaneous reduction in fluid intake, treatment can lead to water retention and/or hyponatraemia (headache, nausea/vomiting, weight gain and in serious cases convulsions). Elderly patients, patients with low plasma sodium levels and patients with high 24-hour urine volumes (above 2.8 to 3 litres) have an increased risk of developing hyponatraemia.
Minirin 0,1 mg/ml nasal spray may cause bronchospasm due to the presence of benzalkonium chloride in this product.

In patients with urgency/urge incontinence, organic causes for increased micturition frequency or nocturia (e.g. benign prostatic hyperplasia, urinary tract infection, bladder stones/tumours), polydipsia or poorly controlled diabetes mellitus, the specific cause of the symptoms should be dealt with primarily.
Treatment with desmopressin should be carefully adjusted during acute illness characterised by fluid and/or electrolyte imbalance such as systemic infections, fever and gastroenteritis.
There is some evidence from post-marketing data for the occurrence of severe hyponatraemia in association with the nasal spray formulation of desmopressin, when it is used in the treatment of cranial diabetes insipidus.

Note
For intranasal use only.
Laboratory tests for monitoring the patients include urine volume and osmolality. In some cases plasma osmolality may be required.

Stability and storage:
MINIRIN nasal spray should be stored in room temperature (max 25°C).

Legal category
Prescription only medicine.

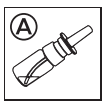
Package quantities:
1 x 2.5ml
1 x 5ml

Marketing Authorization Holder:
Ferring SA
St. Prex, Switzerland

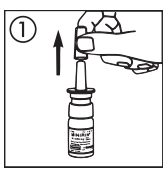
Manufacturer:
Ferring GmbH
Kiel, Germany

January 2007

Read this information before you use MINIRIN nasal spray.
Note! Before you use MINIRIN nasal spray the first time. You should prime the pump by pressing it downwards 4 times, or until an even spray is obtained. If you have not used MINIRIN nasal spray during the last week, it is necessary to prime it again by pressing it downwards once, or until an even spray appears. IMPORTANT! The end of the tube inside the bottle must always be submerged in the liquid when you use the spray (see figure A).

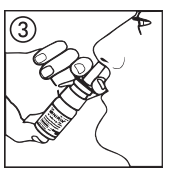


Instruction for use:

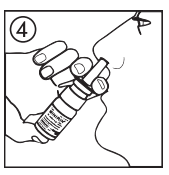


Remove the protective cap from the applicator.

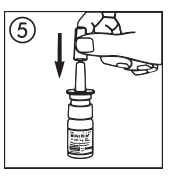
Hold the bottle according to the figure.



Tilt your head backwards slightly. Insert the nasal applicator into one nostril according to figure 3. Hold your breath as you administer the dose.



If more than 1 dose is prescribed by your physician, repeat the administration in the other nostril. Use alternative nostrils for each additional dose.



Replace the protective cap Always store the bottle upright.

THIS IS A MEDICINE
- A MEDICINE IS A PRODUCT WHICH AFFECTS YOUR HEALTH. AND ITS CONSUMPTION CONTRARY TO INSTRUCTIONS IS DANGEROUS FOR YOU.
- STRICTLY FOLLOW THE DOCTOR'S PRESCRIPTION, THE METHOD OF USE AND THE INSTRUCTIONS OF THE PHARMACISTS WHO SOLD THE MEDICINE.
- THE DOCTORS AND THE PHARMACIST ARE EXPERTS IN MEDICINE, ITS BENEFITS AND RISKS.
- DO NOT BY YOURSELF INTERRUPT THE PERIOD OR TREATMENT PRESCRIBED FOR YOU.
- DO NOT REPEAT THE SAME PRESCRIPTION WITHOUT CONSULTING YOUR DOCTOR.
- KEEP THE MEDICINE OUT OF REACH OF CHILDREN.

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mct
AB Malmö Centraltryckeri.
Postadress: Box 16023, 200 25 Malmö, Sweden
Besöksadress: Höjdrodergatan 16, 212 39 Malmö
Tel +46 40 62 50 300. Fax +46 40 62 50 399.