MINIRIN Melt ® 60 , 120 , 240 mcg
MINIRIN® 60 micrograms, 120 micrograms, 240 micrograms oral lyophilisate

FERRING

QUALITATIVE AND QUANTITATIVE COMPOSITION
Each oral lyophilisate MINIRIN® 60 micrograms contains 67 µg desmopressin acetate equivalent to 60 µg desmopressin.
Each oral lyophilisate MINIRIN® 120 micrograms contains 135 µg desmopressin acetate equivalent to 120 µg desmopressin.
Each oral lyophilisate MINIRIN® 240 micrograms contains 270 µg desmopressin acetate equivalent to 240 µg desmopressin.
Active ingredient: Desmopressin acetate

PHARMACEUTICAL FORM
Oral lyophilisate (melt tablet)
Appearance:
60 micrograms: white, round oral lyophilisate imprinted with one drop on one side
120 micrograms: white,round oral lyophilisate imprinted with two drops on one side
240 micrograms: white, round oral lyophilisate imprinted with three drops on one side

CLINICAL PARTICULARS
Therapeutic indications:
-Treatment of primary nocturnal enuresis (from 5 years of age)
-Symptomatic treatment of nocturia (at least twice a night urine production) in adults, in connection with nocturnal polyuria.
-Central diabetes insipidus

Posology and method of administration
Sublingual use

Primary nocturnal enuresis
An initial dosage of 120 micrograms desmopressin before going to bed is recommended. In cases of insufficient therapy success, the dose can be increased to 240 micrograms. Fluid supply should be reduced.With symptoms of water retention and/or hyponatraemia (headache, nausea/vomiting, weight gain and, in severe cases, cramps), the treatment is to be interrupted until the patient has fully recovered. When continuing treatment, the fluid supply has to be controlled strictly. MINIRIN® is intended for a treatment period of up to 3 months. The necessity of additional treatment should be verified following interruption of administration for at least one week.

Nocturia with nocturnal polyuria
For treatment of nocturia, the recommended initial dose is 60 micrograms desmopressin at bedtime. If this dose is not sufficiently effective after one week, it may be increased up to 120 micrograms and subsequently to 240 micrograms by weekly dose escalations. Reduction of nocturnal fluid supply should be observed. In nocturia patients, a frequency/volume chart should be used to diagnose nocturnal polyuria for at least 48 hours before starting treatment. A night-time urine production exceeding the functional bladder capacity or 1/3 of the 24-hour urine production is regarded as nocturnal polyuria.
In addition, serum sodium levels should be measured before start of treatment.The body weight should be checked over several days at the beginning of treatment and after increase of dose. Simultaneous food intake may reduce the intensity and duration of the antidiuretic effect of low doses of Desmopressin.Treatment of elderly patients is not recommended. If, nevertheless, therapy is to be performed, serum sodium levels should be determined before start of treatment, 3 days after start of treatment, 3 days after a dose increase as well as at other time points deemed necessary.
In the event of signs of water retention and/or hyponatraemia (headache, oedemas, nausea/vomiting, weight gain and, in severe cases, cramps), treatment should be interrupted until the patient has fully recovered. When restarting treatment, strict fluid intake and close monitoring of serum sodium levels should be enforced.If adequate effect is not achieved within 1 week with appropriate dosage, the medication should be discontinued.

Central diabetes insipidus
Adults and children: the dosage is to be adapted individually. The daily dose is normally between 120 micrograms and 720 micrograms. The initial dosage for adults and children should be around 60 micrograms, three times daily, and then adapted to the patient's individual reaction. The maintenance dose for most patients is 60 – 120 micrograms, three times daily.With symptoms of water retention/hyponatraemia, the treatment is to be interrupted, and the dosage is to be adapted.

Contraindications
MINIRIN® is contraindicated with:
-hypersensitivity to desmopressin or any of the other ingredients of the medicinal product
-habitual or psychogeneous polydipsia (resulting in a urine production exceeding 40 mg/kg/24 hours), polydipsia in alcoholics
-known or suspected cardiac insufficiency
-conditions that require therapy with diuretics
-known hyponatraemia
-renal insufficiency with a creatinine clearance below 50 ml/min
-syndrome of inadequate ADH secretion
-patients aged 65 or more if desmopressin used to treat nocturia

Special warnings and precautions for use
Warnings
With treatment of primary nocturnal enuresis and nocturia, the fluid supply is to be reduced to a minimum from one hour before administration until the next morning (at least 8 hours following administration)
Treatment without simultaneous restriction of fluid supply can lead to water retention and/or hyponatraemia with or without accompanying warning symptoms (headache, nausea/vomiting, weight gain) and, in severe cases, to cerebral oedema sometimes associated with clouding of consciousness up to loss of consciousness.

Precautions for use
Desmopressin should be used with caution in patients with mild renal insufficiency.
Serious bladder function disorders and bladder neck obstruction have to be excluded prior to treatment.
Elderly patients and those with low sodium serum levels may show an increased risk of hyponatraemia.
Treatment with desmopressin should be interrupted in cases of upcoming diseases characterised by fluid and/or electrolyte balance disorders.
Precautions for the avoidance of hyponatraemia have to be taken in cases of:
-accompanying treatment with medicinal products that can induce SIADH, e.g. antidepressants, selective serotonin reuptake inhibitors, chlorpromazine and carbamazepine.
-simultaneous treatment with non-steroidal anti-inflammatory drugs.

Interactions with other medicinal products and other interactions
Substances known to induce SIADH, e.g. tricyclic antidepressants, selective serotonin reuptake inhibitors, chlorpromazine, carbamazepine and indomethacine, can increase the antidiuretic effect which can lead to an increased risk of water retention/hyponatraemia. Non-steroidal anti-inflammatory drugs can induce water retention/hyponatremia. Accompanying treatment with loperamide can lead to an increase of the desmopressin plasma concentration to three times the amount, which, in turn, can cause an increased risk of water retention/hyponatremia. Although there are no data on this, other medicinal products which slow down the intestinal transport can have the same effect. Interactions of desmopressin with substances influencing the liver metabolism are improbable since desmopressin does not show any significant metabolism in the liver in in-vitro studies in human microsomes. In-vivo studies on possible interactions have not been performed so far.
A standardised diet with 27 % fat significantly reduces the absorption (amount and duration) of orally administered desmopressin. With respect to the pharmacodynamic characteristics (urine production or osmolality), no significant effect has been reported. With low desmopressin doses, simultaneous food supply can reduce the effect and duration of the antidiuretic effect. In case of concomitant use of oxytocin, an increased antidiuretic effect and reduced uterus perfusion should be taken into account. Clofibrate, indomethacin and carbamazepine may intensify the antiduretic effect of desmopressin whilst glibenclamide may reduce it.

Pregnancy
The medicinal product should be given with caution to pregnant women and monitoring of blood pressure is recommended.
The available data with a limited number of pregnant women (n = 53) with diabetes insipidus show that desmopressin has no negative effect on pregnancy or the health condition of the fetus or newborn. So far, there are no further relevant epidemiological data. Animal experiments show no direct or indirect harmful effects on pregnancy, the development of the embryo or fetus, birth or postnatal development.
MINIRIN ® should only be administered to pregnant women after thoroughly weighing up the risks and benefits.

Lactation
Examinations of the mother's milk of women who had been administered a high dosage of 300 µg desmopressin (intranasal) showed that the amounts of desmopressin that could be transferred to the child are too low to influence the diuresis.

Effects on ability to drive and use machines
None.

Undesirable effects
Treatment without simultaneous limited fluid supply can lead to water retention/hyponatremia with or without accompanying warning symptoms (headache, nausea/vomiting, weight gain and, in serious cases, cramps sometimes associated with somnolence up to prolonged loss of consciousness). This applies particularly to small children up to one year or elderly people, dependant on their overall condition.
Primary nocturnal enuresis and central diabetes insipidus:
Common: Headache, Abdominal pain, nausea.
Very rare: Allergic reactions of the skin, General allergic reactions, Hyponatraemia, Emotional disorders (children).
Nocturia:
Very common: Headache
Common: Hyponatraemia, Sleeplessness, Dizziness, Hypertension, Nausea, Abdominal pain, Dry mouth, Diarrhoea, Pollakisuria, Tiredness, Peripheral oedema, Weight gain

Overdose
a) Symptoms of intoxication
The symptoms of an overdose may occur under the following conditions:
-if the dose administered is too high.
-if there is excessive fluid intake at the same time or shortly after desmopressin administration.
The symptoms are manifested by weight gain (water retention), headaches, nausea and, in severe cases, water intoxication with convulsions sometimes associated with clouding of consciousness up to loss of consciousness. An overdose may occur in particular in infants due to an uncautious drug adjustment.
b) Treatment of intoxication
In case of overdose, depending on its severity, the dose should be reduced, the interval between single doses should be increased or the drug should be discontinued. Suspected cerebral oedema requires immediate admittance to intensive care. Convulsions also require intensive measures. There is no known specific antidote to desmopressin. If diuresis is indicated, saluretics such as furosemide can be used under monitoring of serum electrolytes.

PHARMACEUTICAL PARTICULARS
List of excipients: Gelatin, mannitol (Ph.Eur.), citric acid
Incompatibilities: Not applicable
Shelf life: See outer carton
Special precautions for storage: Store at room temperature max (25°C). Store in the original package.
MARKETING AUTHORIZATION HOLDER: Ferring GmbH, Wittland 11D-24109 Kiel
MANUFACTURER: CATALENT U.K. Swindon Zydis Limited, Swindon, UK
REVISION DATE: January 2011

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 PHARMASIST 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.

Council of Arab Health Ministers
Union of Arab Pharmacists