Desmopress

Tablets.

Chemical Composition\Doses:

Desmopress 0.1:

Each tablet contains 0.1 mg of Desmopressin acetate trihydrate = 0.089 mg of Desmopressin.

Desmopress 0.2:

Each tablet contains 0.2 mg of Desmopressin acetate trihydrate = 0.178 mg of Desmopressin.

Pharmacological Classifications: Hormons (Pituitary & Hypothalamic hormons)

Chemical and Pharmacological Properties:

Indications:

• Central diabetes insipid.

• Primary nocturnal enuresis (from 5years of age)

• Symptomatic treatment of nocturia in adults associated with nocturnal polyuria, i.e. nocturnal urine production exceeding bladder capacity.

Posology and method of administration:

The dosage of Desmopress tablets is individually titrated. Desmopress should always be taken at the same time in relation to food intake, since food intake causes decreased absorption and by that also might influence the effect of desmopressin.

- Central diabetes insipidus .A suitable initial dose for children and adult is (0.1 mg 3times daily). The dosage is then titrated according to the patient's response. According to present clinical experience the daily dose has varied between 0.2 and 1.2mg for most patients 0.1-0.2 mg 3times a day is an optimal dosage regimen. In the event of signs of water retention / hyponatremia the treatment should be interrupted and the dosage should be adjusted.

- Primary nocturnal enuresis; A suitable initial dose is 0.2 mg at bedtime. The dose may be increased up to 0.4 mg if the lower dose is not sufficiently effective ,fluid restriction shall be enforced ,in the event of signs or symptoms of water retention and /or hyponatremia (Headache, nausea/vomiting, weigh gain and in serious cases convulsions). The treatment should interrupted until the patient has completely recovered. When The treatment should be carried out after three months by means of at least one treatment -free week.

- Nocturia:

The recommended initial dose is 0.1 mg at bedtime. If this dose is not sufficiently effective after one week it can be increased up to 0.2 mg and subsequently 0.4 mg by weekly dose escalations. Fluid restriction should be observed. A frequency/ volume chart should be used to diagnose nocturnal polyuria for at least 2 days and nights before starting treatment. A night-time urine production exceeding the functional bladder capacity or exceeding 1/3 of the 24-hour urine production is regarded as nocturnal polyuria.

The initiation of treatment in the elderly (65 years of age and over) is not recommended. Should treatment of these patients be considered, serum sodium should be measured before beginning the treatment and 3 days.

After initiation or increase in dosage and other times during treatment as deemed necessary by the treating Physician.

Should there be signs or symptoms of water retention and /or hyponatraemia (headache, nausea / vomiting, weight gain and in serious cases convulsions) the treatment should be interrupted until the patient has completely recovered .When the treatment is resumed strict fluid restriction is necessary.

If adequate clinical effect is not achieved within 4 weeks following appropriate dose titration the medication should be discontinued .

Contraindication:

Habitual or psychogenic polydipsia (urine production exceeding 40ml /kg /24 hours), known or suspected cardiac insufficiency and other condition that require treatment with diuretics, moderate to severe renal insufficiency (creatinine clearance below 50 ml /min), syndrome of inappropriate ADH secretion (SIADH), known hyponatraemia hypersensitivity to desmopressin or to any of the excipients.

special warnings and precaution for use:

In patients with urgency /urge incontinence, organic causes for increased micturition frequency or nocturia (e.g. benign prostate hyperplasia (BPH), urinary tract infection, bladder stones /tumors), polydipsia and poorly adjusted diabetes mellitus, the specific cause should be treated.

In the treatment of primary nocturnal enuresis and nocturia fluid intake shall be limited to the least possible during the period of one hour before and 8 hours after administration.

Treatment without concomitant reduction in fluid intake can lead to water retention and /or hyponatraemia (Headache, nausea / vomiting, weight gain and in serious cases convulsions)

In clinical trials, higher occurrence of hyponatraemia was found in patients over 65 years. Therefore, the initiation of treatment in the elderly is not recommended, especially not in patients suffering from other conditions that may increase the linklihood of fluid or electrolyte imbalance.

Elderly patients: patients with low serum sodium levels and patients with high 24-hour urine volumes (above 2.8 to 3litres) have an increased risk for hyponatraemia.

Precaution 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 drugs ,which are known to induce ADH, e.g. tricyclic antidepressants selective serotonin reuptake inhibitors , chlorpromazine and carbamazepine.

• Case of concomitant treatment with NSAIDs.

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

Interaction with other medicinal products and other forms of interaction:

Substances that are Known to induce disturbed ADH - secretion, e.g. tricyclic antidepressant substances , selective serotonin reuptake inhibitors, chlorpromazine and carbamazeping may cause an additive antiuretic effect with an increased risk of fluid retention. NSAID's preparations can induce water retention /hyponatraemia.

Concomitant treatment with loperamide may result in three-fold increase in desmopressin plasma concentration, wich may lead to an increased risk of water retention /hyponatraemia.

Although not investigated, other drugs slowing intestinal transport might have the same effect.

Concomitant treatment with dimeticone may result in a decreased absorption of desmopressin.

It is unlikely that desmopressin interacts with pharmaceuticals affecting hepatic metabolism, since desmopressin has not been shown to undergo any significant liver metabolism in vitro studies with human microsomes .However, no formal interaction studies in vivo have been carried out.

A standardized meal with 27% fat taken together with or 1.5 h prior to desmopressin decreased the extent and rate of absorption of desmopressin by about 40%.

No significant effect was observed with respect to pharmacodynamics (urine production or osmolality)

However, it cannot be excluded that some patients may have altered effect at concomitant food intake.

Pregnancy and lactation:

Pregnancy:

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 data, no other relevant epidemiological data are available. Animal studies do not indicate direct or in direct 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 (300 µg intranasal); indicate that desmopressin is transferred to the milk. But that the amount of desmopressin that can be transferred to the child is low and probably less than the amount required to influence dieresis .Whether desmopressin will accumulate in breast milk upon repeated doses has not been studied.

Effects on ability to drive and use machines:

Desmopress has no effect on the ability to drive vehicles and use machines.

Undesirable effects:

Treatment without concomitant reduction of fluid intake may lead to water retention and /or hyponatraemia with or without accompanying warning signs and symptoms (headache, nausea /vomiting, weight again and in serious cases convulsions).

• Primary noctumal enuresis and diabetes insipidus:

System organ class	Frequency	Adverse event
Immune system disorders	Isolated reports	Allergic reaction
Metabolism and Nutrition disorders	Very rare (<1/10 000)	Hyponatraemia
Psychiatric disorders	Very rare (<1/10 000)	Headache
Nervous system disorders	Common (>1/100,<1/10)	Headache
Gastrointestinal disorders	Common (>1/100,<1/10)	Abdominal pain ,nausea
Skin and subcutaneous tissue disorders	Very rare (<1/10 000)	Allergic skin reactions

• Nocturia:

In clinical trials in the treatment of nocturia about 35% of the patients experienced adverse drug reactions during dose-titration. 8% of the patients interrupted in the dose titration bhase due to adverse effects and 2% in the subsequent double -blind phase (0.63%on desmopressin and 1,45% on placebo).

System organ class	Frequency	Adverse event
Metabolism and nutrition disorders	Common (>1/100,<1/10)	Hyponatraemia
Nervous system disorders	Common (>1/100,<1/10)	Headache ,dizziness
Cardiac and vascular disorders	Common (>1/100,<1/10)	Peripheral oedema
Urinary tract disorders	Common (>1/100,<1/10)	Micturition frequency
Gastrointestinal disorders	Common (>1/100,<1/10)	Abdominal pain ,nausea ,dry mouth, weight increase

Overdose:

Over dosage leads to prolonged duration of action with an increased risk of retention and hyponatraemia .The treatment of hyponatraemia must be individual but the following general recommendation may be given.

Hyponatraemia is treated by interrupting the desmopressin treatment and fluid restriction. if the patient has symptoms an infusion of isotonic or hypertonic sodium chloride may be given . When the fluid retention is sever (convulsion and loss of consciousness) furosomide treatment is given .

Toxicity: Even normal doses can in combination with considerable fluid intake cause water intoxication.

Doses from 0.3 µg /kg I.V and 2.4 µg /kg intranasally have caused hyponatraemia and convulsions in children and adults. On the other hand, 40 µg intranasally administered to a5-month –old baby and 80 µg intranasally to a5-year-old gave no symptoms. 4ug administered parenterally to a newborn caused oliguria and weight gain.

Symptoms; Headache, nausea .Fluid retention. Hyponatraemia, oliguria, convulsions, lung oedema.

Pharmacological properties

Pharmacodynamic properties: ATC code; H01BA02 Antidiuretic hormone, ADH

DESMOPRESS contains desmopressin ,a structural analogue of the natural pituitary hormone arginine vasopressin .The difference lies in that the amino group in cysteine has been removed and l-arginine has been substituted by D-arginine .This result in a considerably longer duration of action and a complete lack of pressor effect in the dosages used clinically .

Clinical trials with desmopressin tablets in the treatment of nocturia showed the following;

• A reduction of at least 50% in the mean number of nocturia voids was obtained in 39%of patients with desmopressin compared to 5% of patients with placebo (p<0.0001) .

• The mean number of voids per night decreased by 44% with desmopressin compared to 15% with placebo (p<0.0001)

• The median duration of first undisturbed sleep period increased by 64%with desmopressin compared to 20% with placebo (<0.0001)

• The mean duration of first undisturbed sleep period increased by 2 hours with desmopressin compared to 31 minutes with placebo (p<0.0001).

Pharmacokinetic properties:

The absolute bioavailability after per orally administered desmopressin varies between 0.08 and 0.16%.

Desmopressin exhibits a moderate to high variability in bioavailability, both within and between subjects.

Concomitant use of food decreases the rate and extent of absorption by about 40%

The maximal plasma concentration is reached after 1-1.5 hours .Cmax and AUC do not increase in proportion to the administered dose .The distribution volume is 0.2-0.3 L /kg .Desmopressin does not cross the blood –brain barrier. The mean half –life for desmopressin in the elimination phase is 2-3 hours on average.

In vitro studies with human liver microsomes have shown that no significant amount of desmopressin is metabolized in the liver. It is therefore unlikely that desmopressin is metabolized in the liver in human beings After I.V. injection 45% of the amount of desmopressin is found in the urine within 24hours.

Storage:

Store below 25°C.

Packaging:

Desmopress 0.1: 30 tablets.

Desmopress 0.2: 30 tablets.

THIS IS A MEDICAMENTS

A medicament is a product but unlike any products.
A medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
Follow strictly the doctors prescription, the method of use and the instructions of the pharmacist who sold the medicament.
The doctor and the pharmacist are experts in medicines, their benefits and risks.
Do not by yourself interrupt the period of treatment prescribed.
Do not repeat the same prescription without consulting your doctor.

COUNCIL OF ARAB HEALTH MINISTERS **KEEP MEDICAMENTS OUT OF REACH OF CHILDDREN** ARAB PHARMACISTS ASSOCIATION

Produced by: IDM **International Drug Manufacturing - Syria - Aleppo**