

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

DESMOSPRAY®, Desmopressin Nasal Spray.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

DESMOSPRAY contains 10 micrograms of Desmopressin acetate per actuation.

3 PHARMACEUTICAL FORM

Nasal spray.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DESMOSPRAY is indicated for:

- i) The treatment of nocturia associated with multiple sclerosis where other treatments have failed.
- ii) The diagnosis and treatment of vasopressin-sensitive cranial diabetes insipidus.
- iii) Establishing renal concentration capacity.

4.2 Posology and method of administration

Treatment of Nocturia:

When DESMOSPRAY is used for the treatment of nocturia associated with multiple sclerosis, fluid intake must be limited to a minimum from 1 hour before using the spray at bedtime until the next morning and in any case for a minimum of 8 hours after administration.

For multiple sclerosis patients up to 65 years of age with normal renal function suffering from nocturia the dose is one or two sprays intranasally (10 to 20 micrograms) at bedtime. Not more than one dose should be used in any 24 hour period. If a dose of two sprays is required, this should be as one spray into each nostril.

Treatment of Diabetes Insipidus:

Dosage is individual but clinical experience has shown that the average maintenance dose in adults and children is one or two sprays (10 to 20 micrograms) once or twice daily. If a dose of two sprays is required, this should be as one spray into each nostril.

Diagnosis of Diabetes Insipidus:

The diagnostic dose in adults and children is two sprays (20 micrograms). Failure to elaborate a concentrated urine after water deprivation, followed by the ability to do so after the administration of DESMOSPRAY confirms the diagnosis of cranial diabetes insipidus. Failure to concentrate after the administration suggests nephrogenic diabetes insipidus.

Renal Function Testing:

Recommended doses for the renal concentration capacity test:

Adults: Two sprays into each nostril (a total of 40 micrograms)

Children: (1-15 years): One spray into each nostril (a total of 20 micrograms).

Infants (to 1 year): One spray (10 micrograms).

Adults and children with normal renal function can be expected to achieve concentrations above 700mOsm/kg in the period of 5-9 hours following administration of DESMOSPRAY. It is recommended that the bladder should be emptied at the time of administration.

In normal infants a urine concentration of 600mOsm/kg should be achieved in the 5 hour period following the administration of DESMOSPRAY. The fluid intake at the two meals following the administration should be restricted to 50% of the ordinary intake in order to avoid water overload.

4.3 Contraindications

DESMOSPRAY is contraindicated in cases of:

- syndrome of inappropriate ADH secretion (SIADH)
- known hyponatraemia
- a 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 of DESMOSPRAY.

Before prescribing DESMOSPRAY, the diagnoses of habitual or psychogenic polydipsia (resulting in a urine production exceeding 40mg/kg/24 hours) and alcohol abuse should be excluded.

When used to control nocturia in patients with multiple sclerosis, desmopressin should not be used in patients with hypertension or cardiovascular disease.

Desmopressin should not be prescribed to patients over the age of 65 for the treatment of nocturia associated with multiple sclerosis.

4.4 Special warnings and precautions for use

DESMOSPRAY should only be used in patients where orally administered formulations are not suitable.

When DESMOSPRAY is prescribed, it is recommended:

- to start at the lowest dose
- to ensure compliance with fluid restriction instructions
- to increase dosage progressively, with caution
- to ensure that in children, administration is under adult supervision in order to control the dose intake.

Care should be taken with patients who have reduced renal function and/or cardiovascular disease or cystic fibrosis.

Severe bladder dysfunction and outlet obstruction should be considered before starting treatment.

When DESMOSPRAY is used for the treatment of nocturia associated with multiple sclerosis, periodic assessments should be made of blood pressure and weight to monitor the possibility of fluid overload. Treatment with desmopressin should be interrupted during acute intercurrent illness characterised by fluid and/or electrolyte imbalance (such as vomiting, diarrhoea, systemic infections, fever, gastroenteritis).

In the event of signs or symptoms of water retention and/or hyponatraemia (headache, nausea/vomiting, weight gain and in severe cases, convulsions) treatment should be interrupted until the patient has fully recovered. When restarting treatment, strict fluid restriction should be enforced.

Elderly patients and patients with low serum sodium levels may have an increased risk of hyponatraemia.

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

When used for diagnostic purposes, fluid intake must be limited and not exceed 0.5 litres from 1 hour before until 8 hours after administration.

Following diagnostic testing for diabetes insipidus or renal concentration capacity, care should be taken to prevent fluid overload. Fluid should not be forced, orally or parenterally, and patients should only take as much fluid as they require to satisfy thirst.

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.

Precautions to prevent fluid overload must be taken in:

- 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 under carefully supervised conditions in hospital.

4.5 Interaction with other medicinal products and other forms of interaction

Substances which are known to induce SIADH e.g. tricyclic antidepressants, selective serotonin re-uptake inhibitors, chlorpromazine and carbamazepine, may cause an additive antidiuretic effect leading to an increased risk of water retention and/or hyponatraemia (see 4.4).

NSAIDs may induce water retention and/or hyponatraemia (see 4.4).

4.6 Pregnancy and lactation

Pregnancy:

Data on a limited number (n=53) of exposed pregnancies in women with diabetes insipidus indicate rare cases of malformations in children treated during pregnancy. To date, no other relevant epidemiological data are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development.

Caution should be exercised when prescribing to pregnant women. Blood pressure monitoring is recommended due to the increased risk of pre-eclampsia.

Lactation:

Results from analyses of milk from nursing mothers receiving high dose desmopressin (300 micrograms intranasally) indicate that the amounts of desmopressin that may be transferred to the child are considerably less than the amounts required to influence diuresis.

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effects

Side-effects include headache, stomach pain, nausea, nasal congestion, rhinitis and epistaxis. Isolated cases of allergic skin reactions and more severe general allergic reactions have been reported. Very rare cases of emotional disturbances in children

have been reported. Treatment without concomitant reduction of fluid intake may lead to water retention/hyponatraemia with or without accompanying warning signs and symptoms (headache, nausea/vomiting, weight gain, decreased serum sodium and in severe cases, convulsions).

4.9 Overdose

An overdose of DESMOSPRAY leads to a prolonged duration of action with an increased risk of water retention and/or hyponatraemia.

Treatment:

Although the treatment of hyponatraemia should be individualised, the following general recommendations can be given. Hyponatraemia is treated by discontinuing the desmopressin treatment, fluid restriction and symptomatic treatment if needed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Desmopressin is a structural analogue of vasopressin, with two chemical changes, namely desamination of the N-terminal and replacement of the 8-L-Arginine by D-8-Arginine. These changes have increased the antidiuretic activity and prolonged the duration of action. The pressor activity is reduced to less than 0.01% of the natural peptide as a result of which side-effects are rarely seen.

5.2 Pharmacokinetic properties

Following intranasal administration, the bioavailability of desmopressin is of the order of 10%.

Pharmacokinetic parameters following intravenous administration have been reported as follows:

Total clearance: 2.6ml/ min/kg body wt.

T_½: 55mins

Plasma kinetics of DDAVP in man

H. Vilhardt, S. Lundin, J. Falch

Acta Pharmacol et Toxicol, 1986, 58, 379-381

In vitro, in human liver microsome preparations, it has been shown that no significant amount of desmopressin is metabolised in the liver and thus human liver metabolism *in vivo* is not likely to occur.

It is unlikely that desmopressin will interact with drugs affecting hepatic metabolism, since desmopressin has been shown not to undergo significant liver metabolism in *in vitro* studies with human microsomes. However, formal *in vivo* interaction studies have not been performed.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride EP

Citric Acid Monohydrate EP

Disodium Phosphate Dihydrate EP

Benzalkonium Chloride Solution 50% EP

Purified Water EP.

6.2 Incompatibilities

None known.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store at room temperature (up to 25°C). Protect from light.

6.5 Nature and contents of container

The spray pack comprises of a 10ml amber glass injection vial fitted with a snap-on tamper-proof pre-compression pump spray device, to which a 20mm nasal adaptor is attached. It contains a clear, colourless solution of desmopressin acetate 0.1mg/ml. The fill volume is 7.1ml including overage to allow delivery of 60 doses of 0.1ml.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Ferring Pharmaceuticals Ltd.,
The Courtyard
Waterside Drive
Langley
Berkshire
SL3 6EZ.

8 MARKETING AUTHORISATION NUMBER

PL 03194/0024

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

First authorisation: 1 April 1987
Renewal: 30th April 2002

10 DATE OF REVISION OF THE TEXT

April 2007