SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Desmopressin acetate 200 microgram Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200 micrograms of desmopressin acetate (equivalent to 178 micrograms desmopressin).

Excipients with known effects: lactose monohydrate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

White, round, scored on one side and marked with D2 on the other side.

The tablet can be divided into equal halves.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Vasopressin-sensitive cranial diabetes insipidus.
- Post-hypophysectomy polyuria/polydipsia.
- Primary nocturnal enuresis.

4.2 Posology and method of administration

Posology:
Diabetes Insipidus:
Dosage is individual in diabetes insipidus but clinical experience has shown that the total daily dose normally lies in the range of 200 micrograms to 1200 micrograms. A suitable starting dose in adults and children is 100 micrograms three times daily. This dosage regimen should then be adjusted in accordance with the patient's response. For the majority of patients, the maintenance dose is 100 micrograms to 200 micrograms three times daily.

Post-hypophysectomy polyuria/polydipsia:
The dose of desmopressin acetate tablets should be controlled by measurement of urine osmolality.

Primary nocturnal enuresis:
Children (from 5 years of age) and adults (up to 65 years of age) with normal urine concentrating ability who have primary nocturnal enuresis should take 200 micrograms at bedtime and only if needed should the dose be increased to 400 micrograms.
The need for continued treatment should be reassessed after 3 months by means of a period of at least 1 week without Desmopressin acetate tablets.

Method of administration
For oral use only.

4.3 Contraindications

- Hypersensitivity to desmopressin or any of the excipients as listed in section 6.1.
- Cardiac insufficiency and other conditions requiring treatment with diuretic agents.
- When used to control primary nocturnal enuresis desmopressin acetate tablets should only be used in patients with normal blood pressure.
- Before prescribing desmopressin acetate tablets, the diagnoses of psychogenic polydipsia and alcohol abuse should be excluded.
- Desmopressin should not be prescribed to patients over the age of 65 for the treatment of primary nocturnal enuresis.
- Hyponatraemia
- Syndrome of inappropriate secretion of antidiuretic hormone.

4.4 Special warnings and precautions for use

Care should be taken with patients who have reduced renal function and/or cardiovascular disease or cystic fibrosis. In chronic renal disease the antidiuretic effect of Desmopressin acetate tablets would be less than normal.

When desmopressin acetate tablets are used for the treatment of enuresis, fluid intake must be limited from 1 hour before until 8 hours after administration.

Patients being treated for primary nocturnal enuresis should be warned to avoid ingesting water while swimming and to discontinue desmopressin tablets during an episode of vomiting and/or diarrhoea until their fluid balance is once again normal.

Precautions to prevent fluid overload must be taken in:

- conditions characterised by fluid and/or electrolyte imbalance

- patients at risk for increased intracranial pressure

It is important to monitor body weight and blood pressure during treatment with desmopressin.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose- galactose malabsorption should not take this medicine.

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.

NSAIDs may induce water retention and/or hyponatraemia.

Concomitant treatment with loperamide may result in a 3-fold increase of desmopressin plasma concentrations, which may lead to an increased risk of water retention and/or hyponatraemia. Although not investigated, other drugs slowing transport might have the same effect.

A standardised 27% fat meal significantly decreased the absorption (rate and extent) of a 0.4mg dose of oral desmopressin. Although it did not significantly affect the pharmacodynamic effect (urine production and osmolality), there is the potential for this to occur at lower doses. If a diminution of effect is noted, then the effect of food should be considered before increasing the dose.

4.6 Fertility, 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/foetal 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.

Breast-feeding:

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

Summary of the safety profile:

Gastrointestinal tract:
Stomach pain, nausea, abdominal cramps, vomiting.

Nervous system disorders:
Headache
Very rare; emotional disturbance including aggression in children.

Skin/General:
Allergic skin reactions and more severe general allergic reactions.
Treatment with desmopressin without concomitant reduction of fluid intake may lead to water retention/hyponatraemia with accompanying symptoms of headache, nausea, vomiting, weight gain, decreased serum sodium and in serious cases, convulsions.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme, website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in Google Play or Apple App store.

4.9 Overdose

An overdose of Desmopressin acetate Tablets 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. Therefore, symptoms such as an increase in body weight, headache, nausea, abdominal cramps and in severe cases cerebral oedema, convulsions and coma may be expected

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vasopressin and analogues, ATC code: H01BA02

In its main biological effects, desmopressin does not differ qualitatively from vasopressin.
However, desmopressin is characterised by a high antidiuretic activity whereas the uterotonic and vasopressor actions are extremely low.
In a modelling study in which intravenous desmopressin was infused over two hours in healthy adult male subjects, the EC_{50} value was calculated as 1.7pg/ml based on urinary osmolality and 2.4pg/ml based on urinary volume.

5.2 Pharmacokinetic properties

Absorption and distribution

The absolute bioavailability of orally administered desmopressin varies between 0.08% and 0.16%. Mean maximum plasma concentration is reached within 2 hours. The distribution volume is 0.2 – 0.32 l/kg. Desmopressin does not cross the blood-brain barrier. The oral terminal half-life varies between 2.0 and 3.11 hours.

After oral administration of a single dose of 2 x 200 micrograms desmopressin tablets to healthy subjects, 25% of the subjects had plasma concentrations of desmopressin above 1pg/ml up to at least 14 hours post dosing.
Bio-transformation
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. Consequently, it is also unlikely that desmopressin will interact with drugs affecting hepatic metabolism. However, formal *in vivo* interaction studies have not been performed.

Elimination
About 65% of the amount of desmopressin absorbed after oral administration could be recovered in the urine within 24 hours.

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

Lactose monohydrate

Potato starch

Povidone

Magnesiun stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 30°C. Store in original bottle. Keep the bottle tightly closed. The desiccant should not be removed.

6.5 Nature and contents of container

HDPE bottle with HDPE/LDPE cap and desiccant insert.

Pack sizes: 7, 10, 15, 20, 30, 60, 90, 100 and 250 tablets

Not all pack sizes may be marketed

6.6 Special precautions for disposal

Tablets may be crushed, but must not be suspended in water.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 36687/0277

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04/12/2009

10 DATE OF REVISION OF THE TEXT

12/03/2019