SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

DDAVP® Tablets 0.1mg.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 0.1mg Desmopressin acetate

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Tablet
Uncoated, white, oval, convex tablets scored on one side and engraved '0.1' on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

DDAVP Tablets are indicated for the treatment of vasopressin-sensitive cranial diabetes insipidus or in the treatment of post-hypophysectomy polyuria/polydipsia.

4.2 Posology and method of administration

Treatment of Diabetes Insipidus:
Dosage is individual in diabetes insipidus but clinical experience has shown that the total daily dose normally lies in the range of 0.2 to 1.2mg. A suitable starting dose in adults and children is 0.1mg 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 0.1mg to 0.2mg three times daily.

Post-hypophysectomy polyuria/polydipsia:
The dose of DDAVP Tablets should be controlled by measurement of urine osmolality.

4.3 Contraindications

DDAVP Tablets are contraindicated in cases of cardiac insufficiency and other conditions requiring treatment with diuretic agents.

Before prescribing DDAVP Tablets the diagnoses of psychogenic polydipsia and alcohol abuse should be excluded.

4.4 Special warnings and precautions for use

Care should be taken with patients who have reduced renal function and/or cardiovascular disease. In chronic renal disease the antidiuretic effect of DDAVP Tablets would be less than 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

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 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 and nausea. Isolated cases of allergic skin reactions and more severe general allergic reactions have been reported. Very rare cases of emotional disorders including aggression in children have been reported. 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.

4.9 Overdose

An overdose of DDAVP 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

In its main biological effects, DDAVP does not differ qualitatively from vasopressin. However, DDAVP 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

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.

In *in vitro* studies in human liver microsome preparations, it has been shown that no significant amount of desmopressin is metabolised, 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.

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
Magnesium stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 25°C. Keep the container tightly closed.

6.5 Nature and contents of container

30ml High Density Polyethylene (HDPE) bottle with a tamper-proof, twist-off polypropylene (PP) closure with a silica gel desiccant insert. Each bottle contains 30 or 90 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Ferring Pharmaceuticals Ltd
Drayton Hall
Church Road
West Drayton
UB7 7PS
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 03194/0040

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13th January 1993

10 DATE OF REVISION OF THE TEXT

07/09/2017