SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Octim® Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Desmopressin Acetate 15 micrograms per ml

3. PHARMACEUTICAL FORM

Solution for Injection.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Octim® injection is indicated as follows :

1. To increase Factor VIII:C and Factor VIII:Ag in patients with mild to moderate
haemophilia or von Willebrand's disease undergoing surgery or following trauma.

2. To test for fibrinolytic response

4.2. Posology and Method of Administration

Mild to Moderate Haemophilia and von Willebrand's Disease:
By subcutaneous or intravenous administration.
The dose for adults, children and infants is 0.3 micrograms per kilogram body weight, administered by subcutaneous injection or intravenous infusion.
Further doses may be administered at 12 hourly intervals so long as cover is required. As some patients have shown a diminishing response to successive doses, it is recommended that monitoring of factor VIII levels should continue.
For intravenous infusion, the dose should be diluted in 50ml of 0.9% sodium chloride for injection and given over 20 minutes. This dose should be given immediately prior to surgery or following trauma. During administration of

intravenous Desmopressin, vasodilation may occur resulting in decreased blood pressure and tachycardia with facial flushing in some patients.

Increase of Factor VIII levels are dependent on basal levels and are normally between 2 and 5 times the pre-treatment levels. If results from a previous administration of Desmopressin are not available then blood should be taken pre-dose and 20 minutes post-dose for assay of factor VIII levels in order to monitor response.

Unless contraindicated, when surgery is undertaken tranexamic acid may be given orally at the recommended dose from 24 hours beforehand until healing is complete.

Fibrinolytic Response Testing:
By subcutaneous or intraveonus administration.
The dose for adults and children is 0.3 micrograms per kilogram body weight, administered by subcutaneous injection or intravenous infusion.
For intravenous infusion, the dose should be diluted in 50ml of 0.9% sodium chloride for injection and given over 20 minutes.
A sample of venous blood should be taken 20 minutes after the administration. In patients with a normal response the sample should show fibrinolytic activity of euglobulin clot precipitate on fibrin plates of at least 240mm^2.

4.3. Contra-Indications

Octim® Injection is contraindicated in cases of:
- habitual and psychogenic polydipsia
- unstable angina pectoris
- decompensated cardiac insufficiency
- von Willebrand's Disease Type IIB where the administration of Desmopressin may result
  in pseudothrombocytopenia due to the release of abnormal clotting factors which cause
  platelet aggregation.

Fibrinolytic Response Testing should not be carried out in patients with hypertension, heart disease, cardiac insufficiency and other conditions requiring treatment with diuretic agents.

4.4. Special Warnings and Special Precautions for Use

Precautions to prevent fluid overload must be taken in :
- conditions characterised by fluid and/or electrolyte imbalance
- patients at risk for increased intracranial pressure

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

When repeated doses are used to control bleeding in haemophilia or von Willebrand's disease, 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. Intravenous infusions should not be left up as a routine after surgery. Fluid accumulation can be readily monitored by weighing the patient or by determining plasma sodium or osmolality.

Measures to prevent fluid overload must be taken in patients with conditions requiring treatment with diuretic agents.

Special attention must be paid to the risk of water retention. The fluid intake should be restricted to the least possible and the body weight should be checked regularly.

If there is a gradual increase of the body weight, decrease of serum sodium to below 130mmol/l or plasma osmolality to below 270mOsm/kg, the fluid intake must be reduced drastically and the administration of Octim® Injection interrupted.

During administration of Octim® Injection, it is recommended that the patient's blood pressure is monitored continuously.

Octim® Injection does not reduce prolonged bleeding time in thrombocytopenia.

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 addictive antidiuretic effect leading to an increased risk of water retention and/or hyponatremia.

NSAIDs may induce water retention and/or hyponatraemia.

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/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.

Lactation :
Results from analyses of milk from nursing mothers receiving 300 micrograms Desmopressin intranasally indicate that the amounts of Desmopressin that may be transferred to the child are considerably less than the amounts required to influence diuresis or haemostasis.

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.

During intravenous infusion of OCTIM Injection, vasodilation may occur, resulting in decreased blood pressure and tachycardia with facial flushing. This side effect is normally avoided by infusing the product over 20 minutes.

4.9. Overdose

An overdose of Octim Injection 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 8-D-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.
Like vasopressin, Desmopressin also increases concentrations of Factor VIII:C, Factor VIII:Ag (vWF) and Plasminogen Activator (t-PA).

5.2. Pharmacokinetic Properties

Following intravenous injection, plasma concentrations of Desmopressin follow a biexponential curve. The initial fast phase of a few minutes duration and with a half life of less than 10 minutes is thought mainly to represent the diffusion of Desmopressin from plasma to its volume of distribution. The second phase with a half life of 51-158 minutes represents the elimination rate of Desmopressin from the body.

As a comparison, the half life of vasopressin is less than 10 minutes.

Subcutaneous administration of Desmopressin results in a later Tmax and lower Cmax values but comparable bioavailability.

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. Pre-clinical Safety Data

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

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Sodium Chloride EP
Hydrochloric Acid EP

Water for Injection EP

6.2. Incompatibilities

None.

6.3 Shelf life

48 months.

6.4. Special Precautions for Storage

Store in a refrigerator at 2°C- 8°C and protect from light.

6.5. Nature and Content of Container

Clear Glass ampoules.

6.6. Instruction for Use, Handling and Disposal

The injection is administered by subcutaneous injection or intravenous infusion.
For intravenous infusion, the dose should be diluted in 50ml of 0.9% sodium chloride for injection and given over 20 minutes.

7 MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

PL 03194/0055

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