Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Octostim 15 micrograms/ml Solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution for injection contains 15 micrograms desmopressin acetate equivalent to 13.4 micrograms desmopressin.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection
Uncoloured glass ampoule containing a clear aqueous solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

OCTOSTIM® solution for subcutaneous injection or as intravenous infusion as follows:

- For short-term use to increase factor eight levels in patients with mild to moderate haemophilia or von Willebrand's disease under going surgery or following trauma, and who respond positively to a test dose.
- To test for Fibrinolytic response.

4.2 Posology and method of administration

0.3 micrograms/kg body weight subcutaneously or diluted in physiological saline to 50-100 ml and given as an intravenous infusion over 15-30 minutes. If a positive effect is obtained, the initial OCTOSTIM dose may be repeated 1-2 times with intervals of 6-12 hours. Further repetition of the dose may result in a reduced effect.

In patients with haemophilia A the desired increase of VIII:C is appraised by the same criterion as in the treatment with Factor VIII-concentrate. If the OCTOSTIM infusion does not lead to the desired increase of the concentration of VIII:C in plasma, the treatment may be complemented with administration of factor VIII concentrate. Treatment of haemophilia patients should be conducted in consultation with each patient’s coagulation laboratory.

Determination of coagulation factors and bleeding time before OCTOSTIM-treatment:
Plasma levels of VIII:C and vWF:Ag increase substantially after the desmopressin administration. However it has not been possible to establish any correlation between the plasma concentration of these factors and the bleeding time, either before or after desmopressin. The effect of Desmopressin on the bleeding time should therefore, if possible, be tested in the individual patient.

The bleeding time should be as standardised as possible, e.g. with the use of Simplate II. Determination of bleeding time and plasma levels of the coagulation factors should be conducted in co-operation or consultation with a coagulation laboratory.

Treatment control
The VIII:C concentration must be monitored regularly since in a few cases the effect has been seen to decrease with repeated doses.

In connection with administration of OCTOSTIM the patient's blood pressure must be monitored carefully.

The injection is administered by subcutaneous injection or intravenous infusion. For intravenous infusion the dose (0.3 micrograms/kg body weight) should be diluted in 50-100ml 0.9% sodium chloride for injection (physiological saline) and given over 15-30 minutes.

4.3 Contraindications

OCTOSTIM solution for injection is contraindicated in cases of:

- Habitual and psychogenic polydipsia (resulting in a urine production exceeding 40ml/kg/24 hours).
- History of unstable angina pectoris and/or known or suspected cardiac insufficiency and other conditions requiring treatment with diuretics.
- Known hyponatraemia.
- Von Willebrand's Disease Type IIB.

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 precautions for use

OCTOSTIM solution for injection should be used with caution in:

- Very young or elderly patients.
- Conditions characterised by fluid and/or electrolyte imbalance.
- Patients at risk for increased intracranial pressure.

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

Special warnings:
Special attention must be paid to the risk of fluid retention/hyponatraemia. 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 body weight, decrease of serum sodium to below 130 mmol/l or plasma osmolality to below 270 mOsm/kg body weight, the fluid intake must be reduced drastically and the administration of OCTOSTIM interrupted.

OCTOSTIM does not reduce prolonged bleeding time in thrombocytopenia.

Precautions:
Treatment with Desmopressin should be reassessed during acute intercurrent illnesses and the fluid and electrolyte balance should be carefully monitored, especially in situations with excessive bleeding.

4.5 Interaction with other medicinal products and other forms of interaction

Substances which are known or suspected to induce Syndrome of Inappropriate Antidiuretic Hormone (SIADH) e.g. tricyclic antidepressants, selective serotonin reuptake inhibitors, chlorpromazine and carbamazepine, may cause an additive antidiuretic effect and increase the risk of fluid retention/hyponatraemia. (see 4.4 special Warnings ands Precautions for use).

Non steroidal anti-inflammatory drugs (NSAIDs) may induce fluid retention/hyponatraemia (see section 4.4 special Warnings ands Precautions for use).

4.6 Fertility, pregnancy and lactation

Pregnancy:
Published 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 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.

Lactation:
Results from analyses of milk from nursing mothers receiving a high dose of desmopressin (300 micrograms intranasally), indicate that the amount 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

A few per cent of treated patients can be expected to experience side effects such as fatigue, headache, nausea and abdominal pain.

Common (>1/100)
General: Headache, at high doses fatigue.
Circulation: at high doses: transient fall in blood pressure with a reflex tachycardia and facial flushing at the time of administration.
Gastro Intestinal: Abdominal pain, nausea.

Rare (<1/1000)
General: at high doses: dizziness.

Very rare (<1/10,000)
Metabolism: Hyponatraemia

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

Post marketing experience:
Isolated cases of allergic skin reactions and more severe general allergic reactions have been reported.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2. Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Overdose of OCTOSTIM solution can lead to fluid retention and hyponatraemia.

Treatment:
Although the treatment of hyponatraemia should be individualised, the following general recommendations can be

given: Discontinue the desmopressin treatment, restrict fluid intake and treat symptoms if needed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vasopressin & analogues, ATC code: H01B A02.

OCTOSTIM injection contains desmopressin, a structural analogue of the natural pituitary hormone arginine vasopressin. The difference lies in the desamination of cysteine and substitution of L-arginine by D-arginine. This results in a considerably longer duration of action and a complete lack of pressor effect in the dosages clinically used.

Desmopressin at high dosage, 0.3 micrograms/kg body weight intravenously, leads to a two- to fourfold increase in plasma of factor VIII coagulant activity (VIII:C). Also the content of von Willebrand factor-antigen (vWF:Ag) increases, but to a lesser extent. At the same time there is a release of plasminogen activator (tPA).

Administration of desmopressin has also been shown to lead to a shortening or normalisation of the bleeding time in patients with prolonged bleeding time as in uremia, liver cirrhosis, congenital or drug induced thrombocyte dysfunction and in patients with prolonged bleeding time of unknown etiology.

By administration of desmopressin instead of factor VIII concentrates the risk of transmission of HIV infection and hepatitis virus is avoided.

5.2 Pharmacokinetic properties

Plasma half life varies between 3-4 hours. The duration of the haemostatic effect depends on the half-life for VIII:C which is about 8-12 hours. The bioavailability following subcutaneous injection compared with intravenous administration is about 85%. Maximum plasma concentration after 0.3 micrograms/kg is achieved after approximately 60 minutes and it amounts to 600 pg/ml on average.

5.3 Preclinical safety data

There were no unusual findings during the examination of the safety profile of desmopressin.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Hydrochloric acid (for pH adjustment)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

4 years

6.4 Special precautions for storage

OCTOSTIM solution for injection should be stored at 2° C - 8° C.

6.5 Nature and contents of container

Colourless, Type I glass ampoule. One ampoule contains 1 ml solution.

Pack sizes: 10 x 1 ml.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

For single use only. Discard any unused contents.

7 MARKETING AUTHORISATION HOLDER

Ferring Ireland Ltd.
United Drug House
Magna Drive
Magna Business Park
Citywest Road
Dublin 24

8 MARKETING AUTHORISATION NUMBER

PA 1009/14/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28 April 2006

Date of last renewals: 28 April 2011

10 DATE OF REVISION OF THE TEXT

May 2015