Octostim

Ferring
Injection 15 microg/ml
Factor VIII releasing properties.

Declaration. 1 ml solution contains: Desmopressin acetate 15 µg, sodium chloride 9 mg, hydrochloric acid q.s., and water for injection to 1 ml.

Properties. Octostim contains desmopressin, a structural analogue of the endogenous human pituitary posterior lobe hormone, arginine vasopressin. It differs by omittance of the amino group in cystein and by replacement of L-arginine by D-arginine.

Desmopressin in high dosage, 0.3-0.4 µg/kg body weight intravenously or subcutaneously 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 less extent. At the time there is a release of the plasminogen activator (PA).

The bioavailability following subcutaneous injection relatively to intravenous administration, is about 85%. Maximum plasma concentration following a dose of 0.3 µg/kg, is reached after approximately 60 minutes and amounts to 600 pg/ml on an average. Plasma half life ranges between 3 and 4 hours.

Administration of desmopressin has also shown to lead to shortening or normalization of the bleeding time in patients with prolonged bleeding time as in ureaemia, liver cirrhosis, congenital or drug-induced thrombocyte dysfunction and in patients with prolonged bleeding time of unknown aetiology.

In patients with von Willebrand disease of type IIB, the factor VIII is abnormal and desmopressin may then cause thrombocyte aggregation and thrombocytopenia.

The risk of transmittance of HIV-infection and hepatitis virus as seen for factor VIII concentrates is also avoided by administration of desmopressin.

pH of the solution is about 4.

Indications: Shortening or normalization of a prolonged bleeding time in patients with uraemia, liver cirrhosis, congenital or drug-induced thrombocyte dysfunction and in patients with prolonged bleeding time of unknown aetiology, before an invasive therapeutic or diagnostic operation where a prolonged bleeding time may lead to bleeding complications.

Therapeutic in control of bleeding in patients with uraemia. Bleeding prophylaxis in connection with minor surgical procedures in patients with mild haemophilia A and mild von willebrand disease except type IIB. In exceptional cases, even moderate forms of the diseases can be treated.

Precautions. The drug should be used with caution in patients with a history of heart disease and hypertension and in elderly patients.

Pregnancy. Clinical experience from pregnant women is limited. Experimental data from animal studies have revealed no evidence of a harmful action of desmopressin on the foetus.

Nursing. Information as to whether desmopressin passes into the mother's milk or not, is not available. However, absorption of the intact peptide in the child's gastrointestinal tract is not probable.

Side effects. A few percent of treated patients are expected to experience side effects as fatigue, headache, nausea and abdominal cramp. These side effects are related to the pharmacological effects of the drug and may be prevented or disappear at dose reduction.

Common (>1/100)
General: Fatigue, headache
Circulation: High doses: Transient fall in blood pressure with a reflex tachycardia and facial flushing at the time of administration.
GI: Mild abdominal cramp, nausea
Rare (>1/1000)
High doses without concomitant restriction of the water intake may lead to water retention with accompanying symptoms (weight gain, reduced serum sodium, and, in serious cases, cramps).

Dosage. **Control of bleeding at prolonged bleeding time**. Immediately before the operation 0.3 µg/kg 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 tachphylaxis.

Therapeutic in patients with uraemia. At bleeding 0.3 µg/kg subcutaneously or diluted in 50-100 ml physiological saline and given as an intravenous infusion over 20-30 minutes.

The initial dose may be repeated 1-2 times with intervals of 6-12 hours. Further repetitions of the dose may result in reduced effect.

Bleeding prophylaxis in patients with haemophilia A and von willebrand disease. During 30 minutes immediately before the operation, 0.3 µg Octostim per kg bodyweight is given subcutaneously or as a slow intravenous infusion. The dose should be reduced to 0.2 µg in patients with heart disease and in elderly patients. The solution is diluted in physiological saline to 50-100 ml and is administered over 15-30 minutes.

Desired increase if VIII: C is appraised by the same criterion as in the treatment with factor VIII-concentrate. However, the concentration of VIII: C is expected to increase for 1-2 hours after the infusion. So the effect of Octostim differs from passive supply of factor VIII, where the VIII: C-concentration begins to fall immediately after the administration. If sufficient VIII: C-concentration in plasma is obtained after the initial Octostim dose, further infusions may be given with intervals of 12 hours as long as bleeding prophylaxis is necessary. VIII: C-concentration must be followed up regularly since a reduced effect is seen by repeating doses in a few cases. If the Octostim-infusion does not lead to the desired increase of the VIII: C-concentration in plasma, the treatment may be complemented with supply of factor VIII-concentrate.

Determination of coagulation factor before Octostim treatment. Plasma levels of VIII: C and vWF: Ag increase substantially after desmopressin administration, however it has not been possible to establish any correlation between plasma concentration of these factors and the bleeding time, neither before nor after desmopressin. The effect on the bleeding time by desmopressin should therefore if possible be tested in the individual patient.

Bleeding time test should be carried out as standardized 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 cooperation or consultation with a coagulation laboratory.

Note. At administration of high doses for increase of the content of F VIII in plasma 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. In case of a successive increase of the body weight, serum sodium below 130 mml/l or plasma osmolality below 270 mOsm/kg the fluid intake must be reduced drastically and the administration of Octostim be interrupted. There is no known specific antidote for Desmopressin.

In connection with bleeding control the patients blood pressure and pulse should be checked continuously.

Octostim does not reduce prolonged bleeding time in thrombocytopenia.

Storage. Store in refrigerator.

Precautions. Usage in children. Use in infants and children requires careful fluid intake restriction to prevent possible hyponatremia and water intoxication. Do not use desmopressin injection in infants younger than three months in the treatment of hemophilia A or von Willebrand’s disease.

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