

OCTOSTIM NASAL SPRAY

Desmopressin acetate

Presentation

OCTOSTIM 1.5mg/ml nasal spray, solution. (1ml) A clear, colourless solution containing 1.5mg desmopressin acetate equivalent to desmopressin 1.34mg.

Uses

Actions

Pharmacotherapeutic group: vasopressin and analogues, ATC code HOIBA02.

OCTOSTIM nasal spray solution 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 300µg intranasally generally leads to at least a two-fold 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 the plasminogen activator (PA). The effect on the coagulation profile is of the same magnitude as for 0.2µg/kg intravenously administered desmopressin.

A prolonged bleeding time is shortened to the same extent after 300µg desmopressin intranasally as after an intravenous dose of 0.3µg/kg body weight.

The release of factor VIII after intranasal administration of OCTOSTIM may, according to experience from Swedish blood banks, be used for preparation of factor VIII concentrate with increased content of VIII:C but in other respects with unchanged *in vitro* and *in vivo* properties. The yield of factor VIII:C will increase two- to four-fold after desmopressin stimulation in blood donors. No residues of desmopressin or tranexamic acid have been found in the factor VIII concentrate.

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

Pharmacokinetics

The bioavailability relative to intravenous administration, is 3-5%. Maximum plasma concentration following a dose of 300µg, is reached after approximately 1 hour and amounts to 400 pg/ml on average. Plasma half-life is about 3 hours.

Indications

OCTOSTIM nasal spray solution is indicated as follows:

- Therapeutic control of bleeding and bleeding prophylaxis in patients with mild haemophilia A and von Willebrand's disease who respond positively to the test dose. In exceptional cases, even moderate forms of the diseases can be treated.
- Shortening or normalisation of prolonged bleeding time as a consequence of thrombocyte dysfunction in patients who respond positively to a test dose.
- Factor VIII-release in plasma donors. Should not be given more than once every second week.

Dosage and Administration

1 dose of spray provides 0.1ml, which corresponds to 150µg desmopressin acetate.

Therapeutic control of bleeding or bleeding prophylaxis

300µg (1 dose of spray in each nostril) is given at bleeding or half an hour before the operation.

The dose may be repeated every 12th hour for a maximum of 2-3 days. For surgical procedures parenteral administration of desmopressin is primarily recommended.

A desired increase of 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 administration. The effect of OCTOSTIM thus differs from a passive supply of factor VIII, where the VIII:C-concentration begins to fall immediately after the administration.

Plasma levels of VIII:C and vWF:Ag increase substantially after 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. Determination of bleeding time and plasma levels of the coagulation factors should be conducted in co-operation or consultation with a coagulation laboratory.

Blood donation

300µg (1 dose of spray in each nostril) 60-90 minutes before tapping.

Contraindications

OCTOSTIM nasal spray solution is contraindicated in cases of:

- habitual and psychogenic polydipsia
- cardiac insufficiency and other conditions requiring treatment with diuretic agents
- von Willebrand's disease type IIB
- hypersensitivity to the preservative (chlorobutanol)

Warnings and Precautions

OCTOSTIM nasal spray solution should be used with caution in:

- very young and elderly patients
- conditions characterised by fluid and/or electrolyte imbalance
- patients at risk for increased intracranial pressure

Special attention must be paid to the risk of water retention/hyponatremia. In case the patient experiences increases body weight, persistent headache and nausea, serum sodium must be checked. Should there be a 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 nasal spray solution does not reduce prolonged bleeding time in thrombocytopenia. When used for blood donation, to compensate for the increased release of plasminogen activator due to OCTOSTIM nasal spray solution, 50mg tranexamic acid is added to plasma in the blood bag.

Use in pregnancy and lactation

Pregnancy

Reproduction studies performed in rats and rabbits with doses more than 100 times the human dose have revealed no evidence of a harmful action of desmopressin on the foetus. One investigator has reported 3 cases of malformations in children to mothers suffering from diabetes insipidus and receiving desmopressin during pregnancy. However, several other published reports comprising more than 120 cases show that women treated with desmopressin during pregnancy have given birth to normal children. Furthermore a review of a very large data set identifying 29 children who have been exposed to desmopressin during the full pregnancy shows no increase in the malformation rate in the children born.

Lactation

Results from analyses of milk from nursing mothers receiving high dose desmopressin (300µg intranasally), indicate that the amounts of desmopressin that may be transferred to the child are considerably less than the amounts required to influence diuresis.

Effects on ability to drive and use machines

None.

Adverse Effects

Common (>1/100)

General

Headache

Circulation

Transient tachycardia

GI

Stomach pain, nausea

Skin

Facial flush

Upper respiratory

Nasal congestion/rhinitis, epistaxis

Eye

Eye redness

Flush usually occurs in the face and is transient.

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

Post marketing experience

Isolated cases of allergic skin reactions and more severe general allergic reactions have been reported.

Interactions

Substances which are known to release antidiuretic hormone, e.g. tricyclic antidepressants, chlorpromazine and carbamazepine may cause an additive antidiuretic effect leading to an increased risk of water retention/hyponatremia.

Indomethacin increases the urine concentrating effect of desmopressin without influencing the duration. The effect is probably without any clinical significance.

Overdosage

Overdose of OCTOSTIM nasal spray solution can lead to water retention and hyponatremia.

Treatment

Although the treatment of hyponatremia should be individualised, the following general recommendations can be given. Asymptomatic hyponatremia is treated by discontinuing the desmopressin treatment and fluid restriction. Infusion of isotonic or hypertonic sodium chloride may be added in cases with symptoms. When the water retention is severe (convulsions and unconsciousness) treatment with furosemide should be added.

Pharmaceutical Precautions

List of excipients

Chlorobutanol hemihydrate, Sodium Chloride, Hydrochloric Acid, Purified Water.

Incompatibilities

Not applicable.

Shelf-life

3 years.

Special precautions for storage

OCTOSTIM nasal spray solution should be stored at 2°C-8°C.

Instructions for use/handling

Before OCTOSTIM nasal spray solution is used for the first time, the pump must be primed by pressing it downwards 4 times or until an even spray is obtained. When the spray has not been used during the last week it is necessary to prime the pump again by pressing it downwards once, or until an even spray appears.

When the nasal spray is used it is important to make sure that the end of the dip tube inside the bottle is always submerged in the liquid and that the nasal applicator is inserted parallel to the dorsal of the nose at the same time as the head is leaning slightly backwards.

The bottle should always be stored in an upright position.

Medicine Classification

Prescription Medicine.

Package Quantities

Brown Type I glass vial (precompression pump).

Pack size: 2.5ml (about 25 doses).

OCTOSTIM nasal spray is actuated by a manual dose pump without propellant. The spray pump is designed to deliver 100µl solution (= 150µg desmopressin acetate) per actuation.

Further Information

Preclinical safety data

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

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