PRESCRIBING INFORMATION

This prescribing information is intended for international use only and is based on the Summary of Product Characteristics (SPC) for IMMUNATE approved under mutual recognition procedure (MRP) in certain member states of the European Union. Please always refer to the locally approved Prescribing Information before using the product.

IMMUNATE

Powder and solvent for solution for injection

COMPOSITION

Active Substance: Human coagulation Factor VIII/Human von Willebrand Factor (VWF:RCo) 250 IU FVIII/190 IU VWF, 500 IU FVIII/375 IU VWF or 1000 IU FVIII/750 IU VWF per vial.

The specific activity of IMMUNATE is 70 ± 30 IU FVIII/mg protein.

Produced from the plasma of human donors.

Excipients: *Powder:* human albumin, glycine, sodium chloride, sodium citrate, lysine hydrochloride, calcium chloride. *Solvent:* SWFI

INDICATIONS

Treatment and prophylaxis of bleeding in patients with congenital (haemophilia A) or acquired factor VIII deficiency.

Treatment of bleeding in patients with von Willebrand's disease with factor VIII deficiency, if no specific preparation effective against von Willebrand's disease is available, and when desmopressin (DDAVP) treatment alone is ineffective or contra-indicated.

POSOLOGY

Dosage in Haemophilia A

The dose and duration of the substitution therapy depend on the severity of the factor VIII deficiency, on the location and extent of the bleeding and on the patient's clinical condition.

The required dose is determined using the following formula:

Required units = body weight (kg) x desired factor VIII rise (%) x 0.5

The amount and frequency of administration should be adapted to the clinical response in the individual case. Under certain circumstances (e.g. presence of a low titre inhibitor) doses larger than those calculated using the formula may be necessary.

The product should be used with caution in children less than 6 years of age, who have limited exposure to factor VIII products, as there are limited clinical data available for this patient group.

<u>Long-term prophylaxis</u>
For long term prophylaxis against bleeding in patients with severe haemophilia A, the usual doses are 20 to 40 IU of factor VIII per kg body weight at intervals of 2 to 3 days. In some

cases, especially in younger patients, shorter dosage intervals or higher doses may be necessary.

Dosage in von Willebrand's disease
Replacement therapy with Immunate to control haemorrhages follows the guidelines given for haemophilia A.
Since Immunate contains a relatively high amount of factor VIII in relation to vWF, the treating physician should be aware that continued treatment may cause an excessive rise in factor VIII:C, which can lead to an increased risk of thrombosis.

For more information on posology see full SPC.

CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients.

WARNINGS AND PRECAUTIONS FOR USE

Allergic type hypersensitivity reactions are possible with Immunate. If symptoms of hypersensitivity occur, patients should be advised to discontinue use of the medicinal product immediately and contact their physician. In case of shock, standard medical treatment for shock should be implemented.

Patients with Haemophilia A
Inhibitors
The formation of neutralising antibodies (inhibitors) to factor VIII is a known complication in the management of patients with haemophilia A. The risk of developing inhibitors is correlated to the exposure to factor VIII, this risk being highest within the first 20 exposure days. Rarely, inhibitors may develop after the first 100 exposure days. Cases of recurrent inhibitor (low titre) have been observed after switching from one factor VIII product to another in previously treated patients with more than 100 exposure days who have a previous history of inhibitor development. Therefore, it is recommended to monitor all patients carefully for inhibitor occurrence following any product switch.

Patients with von Willebrand’s disease
Inhibitors
Patients with von Willebrand disease, especially type 3 patients, may develop neutralizing antibodies (inhibitors) to von Willebrand factor. If the expected VWF:RCo activity plasma levels are not attained, or if bleeding is not controlled with an appropriate dose, an appropriate assay should be performed to determine if a von Willebrand factor inhibitor is present. In patients with high levels of inhibitor, von Willebrand factor therapy may not be effective and other therapeutic options should be considered.
Thrombotic events
There is a risk of occurrence of thrombotic events, particularly in patients with known clinical or laboratory risk factors. Therefore, patients must be monitored for early signs of thrombosis. Prophylaxis against venous thromboembolism should be instituted, according to the current recommendations. In patients receiving Immunate, plasma levels of FVIII:C should be monitored to avoid sustained excessive FVIII:C plasma levels, which may increase the risk of thrombotic events.

As the quantity of sodium in the maximum daily dose may exceed 200 mg, it should be accounted for in people on a low sodium diet.

When medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

The measures taken are considered effective for enveloped viruses such as HIV, HBV and HCV and for the non-enveloped virus HAV. The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19. Parvovirus B19 infection may be serious for pregnant women (fetal infection) and for individuals with immunodeficiency or increased erythropoiesis (e.g. haemolytic anaemia).

Appropriate vaccination (hepatitis A and B) should be considered for patients in regular / repeated receipt of human plasma-derived factor VIII products.

Immunate contains blood group isoagglutinins (anti-A and anti-B). In patients with blood group A, B, or AB, haemolysis may occur following repetitive administration at short intervals or following administration of very large doses.

PREGNANCY AND LACTATION

IMMUNATE should be used during pregnancy and lactation only if clearly indicated.

UNDESIRABLE EFFECTS

Undesirable effects possible with human plasma derived factor VIII products:

Hypersensitivity or allergic reactions (which may include angioedema, burning and stinging at the infusion site, chills, flushing, generalised urticaria, rash, headache, hives, pruritus, hypotension, lethargy, nausea, restlessness, tachycardia, tightness of the chest, dyspnoea, tingling, vomiting, wheezing) have been observed rarely and may in some cases progress to severe anaphylaxis (including shock). Patients should be advised to contact their physician if these symptoms occur.
Patients with haemophilia A may develop neutralising antibodies (inhibitors) to factor VIIIPatients with von Willebrand disease, especially type 3 patients, may very rarely develop neutralising antibodies (inhibitors) to von Willebrand factor. Such antibodies may occur in close association with anaphylactic reactions. Therefore, patients experiencing anaphylactic reaction should be evaluated for the presence of an inhibitor.
Haemolysis may occur following administration of large doses to patients with blood group A, B or AB.

Undesirable effects based on reports from clinical trials and on post-marketing experience for IMMUNATE:
From the adverse reactions listed, hypersensitivity has been reported in a clinical trial, all other adverse reactions were reported in post-marketing experience.

Uncommon (≥1/1 000, <1/100): hypersensitivity
Not known (frequency cannot be estimated from the available data): coagulopathy, factor VIII inhibition, restlessness, paraesthesia, dizziness, headache, conjunctivitis, tachycardia, palpitations, hypotension, flushing, pallor, cough, vomiting, dyspnoea, nausea, erythema, hyperhidrosis, neurodermatitis, pruritus, rash, urticaria, myalgia, chest pain, chest discomfort, oedema, chills, injection site reactions, pain, pyrexia.

INCOMPATIBILITIES

This medicinal product must not be mixed with other medicinal products.
Only the provided infusion sets should be used because treatment failure can occur as a consequence of human coagulation factor VIII adsorption to the internal surfaces of some infusion equipment.

Medicinal product subject to medical prescription.

03/2015