PRESCRIBING INFORMATION

This prescribing information is intended for international use only and is based on the Summary of Product Characteristics (SmPC) for ADVATE approved by Centralised Procedure in the European Union. Please always refer to the locally approved Prescribing Information before using the product.

ADVATE
Octocog alfa
Recombinant Human Coagulation Factor VIII

COMPOSITION
Active ingredient: Octocog alfa (recombinant human coagulation factor VIII produced by recombinant DNA technology in Chinese Hamster Ovary cells) 250 IU, 500 IU, 1000 IU, 1500 IU, 2000 IU or 3000IU/vial.

Prepared without the addition of any (exogenous) human- or animal-derived protein in the cell culture process, purification or final formulation.

Excipients: mannitol, sodium chloride, histidine, trehalose, calcium chloride, trometamol, polysorbate 80 and glutathione (reduced).

Solvent: 2 ml or 5 ml of sterilised water for injections (SWFI)
(the 2 ml SWFI is licensed for use with ADVATE 250 IU, 500 IU, 1000 IU or 1500 IU single vial potencies in combination with Baxject II and Baxject III device, the 5 ml solvent is licensed for use with ADVATE 250 IU, 500 IU, 1000 IU, 1500 IU, 2000 IU or 3000 IU single vial potencies in combination with Baxject II and Baxject III device. The solvent vial that accompanies the product vial shall be used for reconstitution).

INDICATIONS
Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital Factor VIII deficiency).

POSOLOGY AND METHOD OF ADMINISTRATION
The dose and duration of the substitution therapy depend on the severity of Factor VIII deficiency, the location and extent of the bleeding and on the patient's clinical condition.

On demand treatment
The calculation of the required dosage of Factor VIII is based on the empirical finding that 1 IU Factor VIII per kg body weight raises the plasma Factor VIII activity by 2 IU/dl. The required dose is determined using the following formula:

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

Prophylaxis
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.

Paediatric population
For on demand treatment, dosing does not differ from adult patients. In patients under the age of 6, doses of 20 to 50 IU of FVIII/kg bw 3 to 4 times weekly are recommended for prophylactic therapy.
Use of 2 ml presentations has not been documented for paediatric subjects < 2 years of age.

For more information on posology and method of administration please refer to the full summary of product characteristics.

CONTRAINDICATIONS
Hypersensitivity to the active substance or to any of the excipients or to mouse or hamster proteins.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Allergic-type hypersensitivity reactions, including anaphylaxis, have been reported with ADVATE. The product contains traces of mouse and hamster proteins. If symptoms of hypersensitivity occur, patients should be advised to discontinue use of the product immediately and contact their physicians. In case of shock, standard medical treatment for shock treatment should be implemented.
Due to the decrease in injection volume for ADVATE reconstituted in 2 ml sterilised water for injections, if hypersensitivity reactions occur there is less time to react by stopping the injection. Therefore, caution is advised during injection of ADVATE reconstituted in 2 ml sterilised water for injections, especially in children.

The formation of neutralising antibodies (inhibitors) to Factor VIII is a known complication in the management of individuals with haemophilia A. The risk of developing inhibitors is correlated to the extent of exposure to Factor VIII, the risk being highest within the first 20 exposure days, and to other genetic and environmental factors. Rarely, inhibitors may develop after the first 100 exposure days. Cases of recurrence of inhibitors (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.

For ADVATE reconstituted with 2 ml sterilised water for injections, misapplication (intra-arterially or paravenously) may lead to mild, short term injection site reactions, such as bruising and erythema.

If central venous access device (CVAD) is required, risk of CVAD-related complications including local infections, bacteremia and catheter site thrombosis should be considered.

After reconstitution, this medicinal product contains 0.45 mmol sodium (10 mg) per vial.

UNDESIRABLE EFFECTS
Clinical studies with ADVATE included 418 subjects with at least one exposure to ADVATE reporting in total 93 adverse drug reactions (ADRs). The ADRs that occurred in the highest frequency were development of neutralising antibodies to factor VIII (inhibitors), headache and fever.

Hypersensitivity or allergic reactions have been observed rarely and may in some cases progress to severe anaphylaxis (including shock).

Development of antibodies to mouse and/or hamster protein with related hypersensitivity reactions may be observed.

Frequency of adverse drug reactions in clinical trials and from spontaneous reporting:
Common (≥1/100 to <1/10): factor VIII inhibition, headache, pyrexia;
Uncommon (≥1/1,000 to <1/100): influenza, laryngitis, lymphangitis, dizziness, memory impairment, syncope, tremor, migraine, dysgeusia, eye inflammation, palpitations, haematoma, hot flush, pallor, dyspnoea, diarrhoea, upper abdominal pain, nausea, vomiting,

pruritus, rash, hyperhidrosis, urticaria, peripheral oedema, chest pain, chest discomfort, chills, abnormal feeling, vessel puncture site haematoma, monocyte count increased, coagulation factor VIII level decreased, haematocrit decreased, abnormal laboratory test, post procedural complication, post procedural haemorrhage, procedural site reaction
Not known (cannot be estimated from the available data): anaphylactic reactions, hypersensitivity, fatigue, injection site reaction, malaise.

Inhibitor Development
Inhibitor development in previously treated patients (PTPs) and in previously untreated patients (PUPs) has been reported.

For more information on undesirable effects please refer to the full summary of product characteristics.

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

MA HOLDER AND MA NUMBER
Baxter AG, Vienna

EU/1/03/271/001-020

Medicinal product subject to medical prescription.

11/2014

Detailed information on this medicinal product is available on the website of the European Medicines Agency (EMA) http://www.ema.europa.eu/