

KOGENATE® Bayer Prescribing Information

(Refer to relevant Summary of Product Characteristics (SmPC) before prescribing)

KOGENATE Bayer 250, 500, 1000 and 2000 IU Powder and solvent for solution for injection.

Presentation: Powder and solvent for solution for injection containing octocog alfa, Recombinant Coagulation Factor VIII (rDNA) (bhk). Product should be reconstituted with accompanying 2.5 ml (250, 500, 1000 IU) or 5.0 ml (2000 IU) water for injections; 250 IU gives approx. 100 IU octocog alfa/ml; 500 IU gives approx. 200 IU octocog alfa/ml; 1000 IU and 2000IU give approx. 400 IU octocog alfa/ml. Also comes with administration set. **Indication:** Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency). This preparation does not contain von Willebrand factor and is therefore not indicated in von Willebrand's disease. **Posology and method of administration:** Calculation of required dose of factor VIII is based on empirical finding that 1 IU factor VIII per kg body weight raises plasma factor VIII activity by 1.5–2.5% of normal activity. Required dosage is determined using following formulae:

I. Required IU = body weight (kg) x desired factor VIII rise (% of normal) x 0.5

II. Expected factor VIII rise (% of normal) = $[2 \times \text{administered IU}] / [\text{body weight (kg)}]$.

Dosage and duration of substitution therapy must be based on patient's needs. The following provides a guide for Factor VIII minimum blood levels.

Haemorrhage: Early haemarthrosis, muscle bleed or oral bleed – factor VIII level required is 20–40% (IU/dl) every 12–24 hours for at least one day until bleeding episode as indicated by pain is resolved or healing achieved. **More extensive haemarthrosis, muscle bleed or haematoma** – factor VIII level required is 30–60% (IU/dl) every 12–24 hours for 3–4 days or more until pain and disability are resolved. **Life threatening bleeds such as intracranial bleed, throat bleed, severe abdominal bleed** – factor VIII level required is 60–100% (IU/dl) every 8–24 hours until threat is resolved.

Surgery: Minor including tooth extraction – factor VIII level required is 30–60% (IU/dl) every 24 hours for at least 1 day until healing is achieved. **Major** – factor VIII level required is 80–100% (IU/dl) (pre- and post-operative) a) by Bolus Infusion: every 8–24 hours until adequate wound healing, then therapy for at least another 7 days to maintain factor VIII activity of 30–60%, b) by Continuous Infusion: raise factor VIII activity pre-surgery with an initial bolus infusion and immediately follow with continuous infusion (in IU/kg/h) adjusting according to patient's daily clearance and desired factor VIII levels for at least 7 days (Continuous infusion, clinical and *in vitro* stability has been demonstrated using ambulatory pumps with a PVC reservoir. KOGENATE Bayer contains low level of polysorbate-80 as an excipient, which is known to increase the rate of di-(2-ethylhexyl)phthalate (DEHP) extraction from polyvinyl chloride (PVC) materials. This should be considered for a continuous infusion administration). Dose and frequency of administration should be adapted to clinical effectiveness in individual case, in certain circumstances larger amounts may be required, especially of initial dose. **Prophylaxis:** doses of 20–60 IU per kg body weight at intervals of 2–3 days in severe haemophilia. In some cases, especially in younger patients, shorter dosage intervals or higher doses may be necessary. **Patients with inhibitors:** If inhibitors present at levels less than 10 BU/ml then administration of additional factor VIII may neutralise inhibitor and permit continued clinically effective therapy. In presence of inhibitor, doses required are variable and must be adjusted according to clinical response and plasma factor VIII activity. In patients with titres above 10 BU or with high anamnestic response, use of (activated) prothrombin complex concentrate (PCC) or recombinant activated factor VII (rFVIIa) should be considered. These therapies should be directed by physicians with experience in the care of patients with haemophilia. **Reconstitution and administration:** Detailed instructions for preparation and administration are contained in the package leaflet. KOGENATE Bayer should be injected intravenously over several minutes. The rate of administration should be determined by the patient's comfort level (maximal rate of injection: 2 ml/min). KOGENATE Bayer can be infused by continuous infusion. The infusion rate should be calculated based on the clearance and the desired FVIII level. **Contra-indications:** Known hypersensitivity to active substance, to mouse or hamster protein or to any of the excipients. **Warnings and precautions:** Allergic type hypersensitivity and anaphylactic reactions, formation of neutralising antibodies. Cases of recurrence of inhibitors (low titre) have been observed after switching from one recombinant factor VIII product to another in previously treated patients with more than 100 exposure days who have a history of inhibitor development. In a clinical study about the use of continuous infusion in surgeries, heparin was used to prevent thrombophlebitis at the infusion site as with any other long term intravenous infusions. Contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially "sodium free". **Interactions:** None known. **Pregnancy and lactation:** No information – use only if clearly indicated. **Undesirable effects:** Common - Inhibitor formation to FVIII [reported commonly in previously untreated patients (PUP)/minimally treated patient (MTP) clinical trials and uncommonly in previously treated patients (PTP) and post-marketing studies (PMS)], infusion site reaction, skin associated hypersensitivity reactions (pruritis, urticaria and rash). Serious side effects - Systemic hypersensitivity reactions reported rarely (including one anaphylactic reaction, nausea, abnormal blood pressure and dizziness). In clinical studies 14% PUPs and 17% minimally treated

paediatric patients developed inhibitors. In clinical studies with 73 PTPs, followed over four years, no de-novo inhibitors were observed. In extensive post-registration studies, involving more than 1000 patients less than 0.2% PTPs developed de-novo inhibitors. In a subset having less than 20 exposure days at study entry, less than 11% developed de-novo inhibitors. Other side effects - In rare cases: infusion related febrile reaction (pyrexia). Possible allergic reactions to constituents e.g. trace amounts of mouse and hamster protein in the preparation exists in certain predisposed patients. Prescribers should consult the SmPC in relation to full side effect information. **Overdose:** No symptoms reported. **Incompatibilities:** Must not be mixed with other medicinal products or solvents. Only the provided components (powder vial with Bio-Set device, pre-filled syringe containing solvent and venipuncture set) should be used for reconstitution and injection because treatment failure can occur as a consequence of human coagulation factor VIII adsorption to the internal surfaces of some infusion equipment. **Special Precautions for Storage:** Store in a refrigerator (2°C-8°C). Do not freeze. Keep vial and the pre-filled syringe in the outer carton in order to protect from light. The product may be stored at ambient room temperature (up to 25°C) for 3 months; the product expires at the end of this 3-month period. After reconstitution the product should be used immediately. Do not refrigerate after reconstitution. For single use only. Any unused solution must be discarded. **Legal Category:** POM. **Package Quantities and Basic NHS Costs:** Single dose vials containing 250 IU, 500 IU, 1000 IU or 2000 IU octocog alfa powder, 2.5ml or 5.0 ml water for injections syringe and administration set. 250 IU £165.00, 500 IU £330.00, 1000 IU £660.00, 2000 IU £1320.00 **MA Number(s):** EU/1/00/143/004-006, 010.

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Kogenate® is a registered trademark of Bayer AG, Germany

Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.gov.uk. Adverse events should also be reported to Bayer Schering Pharma. Tel.: 01635 563500, Fax.: 01635 563703, Email: phdsguk@bayer.co.uk