▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the full Summary of Product Characteristics for how to report adverse reactions.

Refixia 500 IU powder and solvent for solution for injection
Refixia 1000 IU powder and solvent for solution for injection
Refixia 2000 IU powder and solvent for solution for injection

Composition Refixia is a recombinant human factor IX, produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology, covalently conjugated to a 40 kDa polyethylene-glycol (PEG) in the rFIX activation peptide. 500 IU nonacog beta pegol (approximately 125 IU/ml after reconstitution); 1000 IU nonacog beta pegol (approximately 250 IU/ml after reconstitution); 2000 IU nonacog beta pegol (approximately 500 IU/ml after reconstitution); Excipient with known effect: less than 1 mmol sodium (23 mg) per vial.

List of excipients *Powder:* Sodium chloride, Histidine, Sucrose, Polysorbate 80, Mannitol, Sodium hydroxide (for pH adjustment), Hydrochloric acid (for pH adjustment); *Solvent:* Histidine, Water for injections, Sodium hydroxide (for pH adjustment), Hydrochloric acid (for pH adjustment)

Therapeutic indications Treatment and prophylaxis of bleeding in patients 12 years and above with haemophilia B (congenital factor IX deficiency).

Posology and method of administration

Previously untreated patients The safety and efficacy of Refixia in previously untreated patients have not yet been established.

Treatment monitoring Due to the interference of polyethylene glycol (PEG) in the one-stage clotting assay with various aPTT reagents, it is recommended to use a chromogenic assay (e.g. Rox Factor IX or Biophen) when monitoring is needed. If a chromogenic assay is not available, it is recommended to use a one-stage clotting assay with an aPTT reagent (e.g. Cephascreen) qualified for use with Refixia

Prophylaxis 40 IU/kg body weight once weekly. Patients on prophylaxis who forget a dose are advised to take their dose upon discovery and thereafter continue with the usual once weekly dosing schedule. A double dose should be avoided.

On-demand treatment Early haemarthrosis, muscle bleeding or oral bleeding, more extensive haemarthrosis, muscle bleeding or haematoma: a single dose of 40IU/kg Refixia is recommended; Severe or life threatening haemorrhages: a single dose of 80IU/kg Refixia is recommended, additional doses of 40 IU/kg can be given

Surgery Minor surgery including tooth extraction: a single dose of 40IU/kg Refixia is recommended, additional doses can be given if needed. Major surgery: a single pre-operative dose of 80IU/kg Refixia is recommended, consider two repeated doses of 40 IU/kg (in 1–3 day intervals) within the first week after surgery, due to the long half-life of Refixia, the frequency of dosing in the post-surgical period may be extended to once weekly after the first week until bleeding stops and healing is achieved.

Paediatric population The dose recommendations in adolescents (12–18 years) are the same as for adults: 40 IU/kg body weight. The long-term safety of Refixia in children below 12 years has not yet been established.

Method of administration Refixia is administered by intravenous bolus injection over several minutes up to a maximum injection rate of 4 ml/min.

Contraindications Hypersensitivity to the active substance or to any of the excipients. Known allergic reaction to hamster protein.

Special warnings and precautions for use

Traceability

In order to improve traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity Allergic type hypersensitivity reactions are possible with Refixia. If symptoms of hypersensitivity occur, patients should be advised to discontinue use of the medicinal product immediately and contact their physician.

Inhibitors After repeated treatment with human coagulation factor IX (rDNA) products, patients should be monitored for the development of neutralising antibodies (inhibitors). Patients experiencing allergic reactions should be evaluated for the presence of an inhibitor. It should be noted that patients with factor IX inhibitors may be at an increased risk of anaphylaxis with subsequent challenge with factor IX. The initial administrations of factor IX should, according to the treating physician's judgement, be performed under medical observation where proper medical care for allergic reactions could be provided.

Interaction with other medicinal products and other forms of interaction No interactions of human coagulation factor IX (rDNA) products with other medicinal products have been reported.

Undesirable effects Common (≥ 1/100 to < 1/10): nausea, fatigue, pruritus, injection site reactions; Uncommon (≥ 1/1,000 to < 1/100): hypersensitivity, palpitations, hot flush; Unknown: anaphylaxis, inhibitors. Hypersensitivity or allergic reactions have been observed rarely with recombinant factor IX products. In some cases, these reactions have progressed to severe anaphylaxis. Very rarely development of antibodies to hamster protein with related hypersensitivity reactions has been observed.

Overdose Overdoses up to 169 IU/kg have been reported in clinical trials. No symptoms associated with overdoses have been reported.

Shelf life: *Unopened* 2 years in the refrigerator or up to 30°C for a single period not exceeding 6 months
After reconstitution 24 hours in a refrigerator (2°C – 8°C) or 4 hours at room temperature (≤ 30°C).

Way of delivery*:* Medical prescription.

Marketing authorisation holder Novo Nordisk A/S;Novo Allé; DK-2880 Bagsværd;Denmark

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For more detailed information please consult the EMA product information.