NovoThirteen® Abbreviated Product Information – October 2020

Name of medicinal product: NovoThirteen 2500 IU powder and solvent for solution for injection. **Composition:** One vial contains catridecacog* (recombinant coagulation factor XIII) (rDNA): 2500 IU per 3 ml, after reconstitution corresponding to a concentration of 833 IU/ml. The specific activity of NovoThirteen is approximately 165 IU/mg protein. **Therapeutic indications:** Long term prophylaxis of bleeding in patients with congenital factor XIII A-subunit deficiency. Treatment of breakthrough bleeding episodes during regular prophylaxis. NovoThirteen can be used for all age groups.
Posology and method of administration: Treatment should be initiated under the supervision of a doctor experienced in the treatment of rare bleeding disorders. The potency of this medicinal product is expressed in international units (IU). Although expressed in the same unitage (IU), the posology of NovoThirteen is different from the dosing schedule of the other FXIII containing products.
Prophylaxis: The recommended dose for prophylactic treatment is 35 IU/kg body weight (bw) once monthly (every 28 days +/- 2 days), administered as an intravenous bolus injection.
Treatment of bleeds: If a breakthrough bleed occurs during regular prophylaxis, it is recommended to treat with a single dose of 35 IU/kg body weight administered as an intravenous bolus injection.
If bleeds occur in a patient who is not on regular prophylaxis, a single dose of 35 IU/kg body weight as an intravenous bolus injection may be administered at the discretion of the treating physician in order to control the bleed.
Based on the actual concentration of NovoThirteen, the dose volume (in millilitres) to be administered can be calculated from the formula below: Dose volume in ml = 0.042 x subject bw (kg). Monitoring NovoThirteen activity levels using a standard FXIII activity assay is recommended. However, if the paediatric patient weighs less than 24 kg, the reconstituted NovoThirteen should be further diluted with 6 ml of sodium chloride 0.9%, solution for injection to handle the dosing of small children. The dose volume for small children can then be calculated by using the below formula: Dose volume in ml = 0.117 x body weight in kilograms.
Minor surgery: It is recommended that minor surgery, including tooth extraction is done in connection with prophylactic dosing. Otherwise, an additional dose can be given if needed. The dose should be based on the FXIII activity levels.
Method of administration: Intravenous use. The preparation should be administered immediately after reconstitution as a slow bolus intravenous injection at a rate not higher than 2 ml/minute.
Contraindications: Hypersensitivity to the active substance or to any of the excipients.
Special warnings and precautions for use: Considering that the posology and the FXIII concentration in NovoThirteen are different from those of the other FXIII containing products, careful attention should be paid to the calculation of the appropriate dose for the individual. The name and the batch number of the administered product should be clearly recorded to improve the traceability of the biological medicinal products. In patients with FXIII deficiency, NovoThirteen is not effective if used for monthly prophylactic treatment of bleeding in patients with congenital FXIII B-subunit deficiency. On-demand treatment of patients not on prophylactic treatment was not studied in clinical development programme. As NovoThirteen contains a recombinant protein it may cause allergic reactions including anaphylactic reactions. Patients should be informed of the early signs of hypersensitivity reactions (including hives, generalised urticaria, tightness of the chest, wheezing, hypotension) and anaphylaxis. If allergic or anaphylactic-type reactions occur, the administration should be immediately discontinued and further treatment with NovoThirteen should not be given. Patients with hepatic impairment and with renal insufficiency requiring dialysis have not been studied in clinical trials.
Inhibitor formation: Inhibitor formation to NovoThirteen therapy has not been detected in clinical trials. Patients known to have neutralising antibodies to FXIII should not be treated with NovoThirteen without close monitoring.
Thromboembolic risk: The reconstituted product must be handled accordingly. Incorrect storage of the product after reconstitution must be avoided as it may result in loss of sterility and in increased levels of activated NovoThirteen. Increased levels of activated

NovoThirteen may increase the risk of thrombosis. In case of predisposition to conditions of thrombosis, caution should be exercised due to the fibrin -stabilising effect of NovoThirteen. There is limited clinical experience in administering NovoThirteen to elderly patients with congenital FXIII deficiency.

Interactions with other medicinal products and other forms of interaction: There are no clinical data available on interaction between NovoThirteen and other medicinal products. Based on the non-clinical study it is not recommended to combine NovoThirteen and recombinant activated FVII (rFVIIa).

Fertility, pregnancy and lactation: There are no studies in pregnant women investigating drug associated risks. Available clinical data do not show any negative effects on the health of the foetus/new-born child or for the pregnant woman. However, NovoThirteen may be considered during pregnancy only if clearly indicated. The excretion of rFXIII in milk has not been studied in animals. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with NovoThirteen should be made taking into

account the benefit of breast-feeding to the child and the benefit of NovoThirteen therapy to the mother. No effects on reproductive organs have been seen in non-clinical studies. There are no human data on potential effects on fertility.
Effects on ability to drive and use machines: NovoThirteen has no influence on the ability to drive and use machines.
Undesirable effects: In clinical trials, NovoThirteen has been administered to 82 patients with congenital factor XIII A -subunit deficiency (3112 doses of NovoThirteen) The most frequent adverse reaction is "headache" reported in 37 % of patients. Non-neutralising antibodies have been seen in 4 of the 82 exposed patients with congenital FXIII deficiency. Antibodies were transient in all patients. **Overdose:** In the reported cases of NovoThirteen overdose up to 2.3 times, no clinical symptoms have been observed. **List of excipients:** Powder: Sodium chloride, Sucrose, Polysorbate 20, L-histidine, Hydrochloric acid (for pH-adjustment), Sodium hydroxide (for pH-adjustment) Solvent: Water for injections. **Incompatibilities:** In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products. **Shelf life:** 2 years. After reconstitution, the medicinal product should be used immediately due to the risk of microbiological contamination. **Special precautions for storage:** Store in a refrigerator (2°C-8°C). Store in original package in order to protect from light. Do not freeze.
Authorisation holder: Novo Nordisk A/S, Novo Allé, DK-2880 Bagsvaerd, Denmark. Date of last revision: October 2020 (last updated SmPC August 2020).
Detailed information on this medicinal product is available on the website of the European Medicines Agency (EMA) http://www.ema.europa.eu/. Novo Nordisk ® is a registered trademark owned by Novo Nordisk A/S. NovoThirteen® is a registered trademark owned by Novo Nordisk Health Care AG, Thurgauerstrasse 36, 8050 Zurich, Switzerland. Tel +41 43 2224300.

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