This Abbreviated Prescribing Information (API) reflects SmPC version as of May 2022. Were changes done to this API as a result of the SmPC change above?
YES ☒ NO ☐

Prepared and updated by Global Medical Affairs Rare Disease based on EU SmPC
Date: June 2022
Veeva ID:
Abbreviated prescribing information
NovoSeven®

Consult Summary of Product Characteristics before prescribing.
Presentation: NovoSeven® 1 mg (50 KIU) powder and solvent (pre-filled syringe) for solution for injection. NovoSeven® 2 mg (100 KIU) powder and solvent (pre-filled syringe) for solution for injection. NovoSeven® 5 mg (250 KIU) powder and solvent (pre-filled syringe) for solution for injection. NovoSeven® 8 mg (400 KIU) powder and solvent (pre-filled syringe) for solution for injection.
Composition: eptacog alfa (activated) is recombinant coagulation factor VIIa (rFVIIa) produced in baby hamster kidney cells (BHK Cells) by recombinant DNA technology, 1 mg/vial, 2 mg/vial, 5 mg/vial, 8 mg/vial (corresponds to 50 KIU/vial, 100 KIU/vial, 250 KIU/vial, 400 KIU/vial). 1mg/ml eptacog alfa (activated) after reconstitution.
List of excipients: *Powder:* Sodium chloride, Calcium chloride dihydrate, Glycylglycine, Polysorbate 80, Mannitol, Sucrose, Methionine, Hydrochloric acid, Sodium hydroxide
Solvent: Histidine, Hydrochloric acid, Sodium hydroxide, Water for injections.
The medicinal product contains less than 1 mmol sodium (23 mg) per injection, indicating that it is essentially 'sodium free'.
Indications: treatment of bleeding episodes and prevention of bleeding in those undergoing surgery or invasive procedures in the following patient groups:

• patients with congenital haemophilia with inhibitors to coagulation factors VIII or IX >5 BU;
• patients with congenital haemophilia who are expected to have a high anamnestic response to factor VIII or factor IX administration;
• patients with acquired haemophilia;
• patients with congenital FVII deficiency;
• patients with Glanzmann's thrombasthenia with past or present refractoriness to platelet transfusions, or where platelets are not readily available

Severe postpartum haemorrhage
NovoSeven is indicated for the treatment of severe postpartum haemorrhage when uterotonics are insufficient to achieve haemostasis.
Posology: *Haemophilia A or B with inhibitors or expected to have a high anamnestic response:*
Mild to moderate bleeding episodes (including home therapy): Early intervention has been shown to be efficacious in the treatment of mild to moderate joint, muscle and mucocutaneous bleeds. Two dosing regimens can be recommended: 1) Two to three injections of 90 µg per kg body weight administered at three-hour intervals. If further treatment is required, one additional dose of 90 µg per kg body weight can be administered 2) One single injection of 270 µg per kg body weight. The duration of the home therapy should not exceed 24 hours. There is no clinical experience with administration of a single dose of 270 µg per kg body weight in elderly patients.
Serious bleeding episodes: An initial dose of 90 µg per kg body weight is recommended and could be administered on the way to the hospital where the patient is usually treated. The following dose varies according to the type and severity of the haemorrhage. Dosing frequency should initially be every second hour until clinical improvement is observed. If continued therapy is indicated, the dose interval can then be increased to 3 hours for 1 - 2 days. Thereafter, the dose interval can be increased successively to every 4, 6, 8 or 12 hours for as long as treatment is judged as being indicated. A major bleeding episode may

be treated for 2 - 3 weeks but can be extended beyond this if clinically warranted. Invasive procedure/surgery: An initial dose of 90 µg per kg body weight should be given immediately before the intervention. The dose should be repeated after 2 hours and then at 2 - 3 hour intervals for the first 24 - 48 hours depending on the intervention performed and the clinical status of the patient. In major surgery, the dose should be continued at 2 - 4 hour intervals for 6 - 7 days. The dose interval may then be increased to 6 - 8 hours for another 2 weeks of treatment. Patients undergoing major surgery may be treated for up to 2 - 3 weeks until healing has occurred. *Acquired Haemophilia:*
NovoSeven® should be given as early as possible after the start of a bleeding episode. The recommended initial dose, administered by intravenous bolus injection, is 90 µg per kg body weight. Following the initial dose of NovoSeven® further injections may be given if required. The duration of treatment and the interval between injections will vary with the severity of the haemorrhage, the invasive procedures or the surgery being performed. The initial dose interval should be 2 - 3 hours. Once haemostasis has been achieved, the dose interval can be increased successively to every 4, 6, 8 or 12 hours for as long as treatment is judged to be indicated. *Factor VII deficiency:*
The recommended dose range is 15 - 30 µg per kg body weight every 4 - 6 hours until haemostasis is achieved. Dose and frequency of injections should be adapted to each individual. Limited clinical experience in long term prophylaxis in paediatric population has been gathered in the paediatric population below 12 years of age, with a severe clinical phenotype. Dose and frequency of injections for prophylaxis should be based on clinical response and adapted to each individual. *Glanzmann's thrombasthenia:*
The recommended dose is 90 µg (range 80 - 120 µg) per kg body weight at intervals of two hours (1.5 - 2.5 hours). At least three doses should be administered to secure effective haemostasis. The recommended route of administration is bolu injection as lack of efficacy may appear in connection with continuous infusion. For those patients who are not refractory, platelets are the first line treatment for Glanzmann's thrombasthenia.
Severe postpartum haemorrhage:
In the management of severe postpartum haemorrhage, appropriate multidisciplinary expertise should be consulted. Dose range and dose interval: the recommended dose range for the treatment of bleeding is 60 – 90 µg per kg body weight administered by intravenous bolus injection. Peak coagulant activity can be expected at 10 minutes. A second dose can be administered based on clinical response of the individual patient. It is recommended that in case of insufficient haemostatic response, a second dose can be administered after 30 minutes.
Contraindications: Hypersensitivity to the active substance, or to any of the excipients, or to mouse, hamster or bovine protein.
Special warnings and precautions for use: In severe postpartum haemorrhage and pregnancy, the clinical conditions (delivery, severe haemorrhage, transfusion, DIC, surgery/invasive procedures and coagulopathy) are known contributing factors to the thromboembolic risk; and in particular venous thromboembolic risk associated with the administration of NovoSeven.
Interaction with other medicinal products and other forms of interaction: The risk of a potential interaction between NovoSeven® and coagulation factor concentrates is unknown. Simultaneous use of prothrombin complex concentrates, activated or not, should be avoided. Antifibrinolytics have been reported to reduce blood loss in association with surgery in haemophilia patients, especially in orthopaedic surgery and surgery in regions rich in fibrinolytic activity, such as the oral cavity. Antifibrinolytics are also used to reduce blood loss in women with postpartum haemorrhage. Experience with concomitant administration of antifibrinolytics and rFVIIa treatment is however limited. Based on a non-clinical study it is not recommended to combine rFVIIa and rFXIII. There are no clinical data available on interaction between rFVIIa and rFXIII.
Fertility, pregnancy and breast-feeding
As a precautionary measure, it is preferable to avoid the use of NovoSeven® during pregnancy. Data from non-clinical studies as well as post-marketing data show no indication that NovoSeven® has a harmful effect on male or female fertility. Limited data from exposed pregnancies did not show any adverse effect on pregnancy or on the health

of foetus/new-born child. It is unknown whether NovoSeven® is excreted in human breast milk

Undesirable effects: The most frequent adverse drug reactions (ADR) are pyrexia and rash (uncommon: ≥ 1/1,000 to < 1/100), and the most serious adverse drug reactions include venous thromboembolic events (uncommon: ≥ 1/1,000 to < 1/100) and arterial thromboembolic events (rare: ≥ 1/10,000 to < 1/1,000).

The frequencies of both serious and non-serious adverse drug reactions are listed by system organ class: Blood and lymphatic system disorders: *Rare:* Disseminated intravascular coagulation, related laboratory findings, including elevated levels of D-dimer and decreased levels of Anti Thrombin (AT) and coagulopathy. Gastrointestinal disorders: *Rare:* nausea. General disorders and administration site conditions: *Uncommon:* ADRs are decreased therapeutic response and pyrexia. *Rare:* ADR is injection site reaction including injection site pain. Immune system disorders: Hypersensitivity is *Rare*; anaphylactic reaction frequency is *not known*. Investigations: *Rare:* increased fibrin degradation products, increase of alanine aminotransferase, alkaline phosphatase, lactate dehydrogenase and prothrombin. Nervous system disorders: *Rare:* headache, skin and subcutaneous tissue disorders: *Uncommon:* Rash (including allergic dermatitis and rash erythematous), pruritus and urticaria. Unknown frequency: flushing and angioedema. Vascular disorders: *Uncommon:* venous thromboembolic events (deep vein thrombosis, thrombosis at i.v. site, pulmonary embolism, thromboembolic events of the liver including portal vein thrombosis, renal vein thrombosis, thrombophlebitis, superficial thrombophlebitis and intestinal ischaemia). *Rare:* Arterial thromboembolic events (myocardial infarction, cerebral infarction, cerebral ischaemia, cerebral artery occlusion, cerebrovascular accident, renal artery thrombosis, peripheral ischaemia, peripheral arterial thrombosis and intestinal ischaemia), Angina pectoris. *Unknown:* Intracardiac thrombus.

Inhibitory antibodies: In post-marketing experience, there have been no reports of inhibitory antibodies against NovoSeven® or FVII in patients with haemophilia A or B. In factor VII deficiency clinical trials: formation of antibodies against NovoSeven® and FVII is the only ADR reported (common). Development of inhibitory antibodies to NovoSeven® has been reported in a post-marketing observational registry of patients with congenital FVII deficiency.

Reporting of suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. **Overdose:** Four cases of overdose have been reported in patients with haemophilia in 16 years. The only complication reported in connection with an overdose was a slight transient increase in blood pressure in a 16 year-old patient receiving 24 mg rFVIIa instead of 5.5 mg. No cases of overdose have been reported in patients with acquired haemophilia or Glanzmann's thrombasthenia. In patients with factor VII deficiency, where the recommended dose is 15 – 30 µg/kg rFVIIa, one episode of overdose has been associated with a thrombotic event (occipital stroke) in an elderly (> 80 year) male patient treated with 10 – 20 times the recommended dose. In addition, the development of antibodies against NovoSeven® and FVII has been associated with overdose in one patient with factor VII deficiency. The dose schedule should not be intentionally increased above the recommended doses due to the absence of information on the additional risk that may be incurred.

Administration: NovoSeven® (eptacog alfa activated) is administered intravenously over 2 – 5 minutes.

Caution: Some needleless connectors with an internal spike used with central venous access devices (CVADs) may be incompatible with the pre-filled glass syringe and prevent administration. Therefore, use of an alternative sterile 10ml luer-lock plastic syringe may be required for withdrawal and injection of the reconstituted solution. Follow the instructions for use for the CVAD and needleless connector.

Storage and shelf life:

The shelf life for the product packed for sale is 3 years when the product is stored below 25°C.

<u>In vial:</u>

After reconstitution, chemical and physical stability has been demonstrated for 6 hours at 25°C and 24 hours at 5°C. From a microbiological point of view, the product should be used immediately. If not used immediately, storage time and storage conditions prior to use are the responsibility of the user and should not be longer than 24 hours at 2°C – 8°C, unless reconstitution has taken place in controlled and validated aseptic conditions. The reconstituted solution should be stored in the vial.

In syringe (50 ml polypropylene) in hospital settings only:

Reconstitution must take place in controlled and validated aseptic conditions by adequately trained staff. Under these conditions, chemical and physical stability has been demonstrated for 24 hours at 25°C when stored in a 50 ml syringe (polypropylene). If not used immediately, the conditions prior to use are the responsibility of the user and the in-use storage time must not be longer than as stated above.

Procedure for pooling of vials for hospital use only:

During in vitro studies, the chemical and physical in-use stability has been demonstrated for 24 hours at 25°C in a 50 ml syringe (polypropylene). Compatibility with the product was demonstrated for the system consisting of a 50 ml syringe (polypropylene), a 2 m infusion tube (polyethylene) and an in-line filter with a 5 micrometer pore size. The syringe with adequately reconstituted product can be used for administration in a CE-marked infusion pump (accepting a 50 ml syringe), for details on pooling the vials (hospital use only) please refer to the SmPC as of May 2022. The infusion pump must only be operated by trained hospital personnel.

Legal category: Prescription-only medicine (POM). MARKETING AUTHORISATION NUMBERS: NovoSeven 1 mg (50 KIU): EU/1/96/006/008. NovoSeven 2 mg (100 KIU): EU/1/96/006/009. NovoSeven 5 mg (250 KIU): EU/1/96/006/010. NovoSeven 8 mg (400 KIU): EU/1/96/006/011. **Authorisation holder:** Novo Nordisk A/S, Bagsvaerd, Denmark. **Date of last revision *SMPC*:** May 2022. **For more detailed information please consult the EMEA product information.** Novo Nordisk® is a registered trademark owned by Novo Nordisk A/S. NovoSeven® is a registered trademark owned by Novo Nordisk Health Care AG, The Circle 32/38, 8058 Zürich, Switzerland, Tel +41432224300.