<date>

NovoSeven (eptacog alfa): manufacturing issue leading to supply shortage

Dear Healthcare professional,

Novo Nordisk A/S [affiliate to include country specific information to reflect global or local company name] in agreement with the European Medicine Agency and the <National Competent Authority> would like to inform you of the following:

Summary

- **A manufacturing issue caused some vials of NovoSeven 1mg and 2mg to be potentially under-filled, causing the reconstituted final product, to be of lower concentration. This issue affected some products manufactured for Spain, Italy, Latvia, Czechia, Lithuania and Austria. The manufacturing issue has now been resolved.**
- **This manufacturing issue, combined with release delays from the packaging line and continued capacity constraints which are not related to the manufacturing issue, is expected to cause intermittent shortages at least throughout 2024 for NovoSeven 1mg and 2mg.**
- **In a shortage situation, Healthcare professionals (HCPs) should ensure that patients using NovoSeven 1mg and 2mg are safely switched to an alternative strength until supply is restored or to suitable alternatives, if appropriate, based on their clinical judgment and according to the local label recommendations.**

Background

NovoSeven is a recombinant, activated Factor 7 which is is indicated for the treatment of bleeding episodes and for the prevention of bleeding in those undergoing surgery or invasive procedures in patients with:

- congenital haemophilia with inhibitors to coagulation factors VIII or IX > 5 Bethesda Units (BU);
- congenital haemophilia who are expected to have a high anamnestic response to factor VIII or factor IX administration;
- acquired haemophilia;
- congenital FVII deficiency;
- 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.

NovoSeven is available as powder and solvent for solution for injection in 4 different strengths (1, 2, 5 and 8 mg).

A manufacturing issue on a filling line caused some vials of NovoSeven 1mg and 2mg to be potentially under-filled. The root cause of the under-filled vial issue has been identified and the filling line will resume operation. NovoSeven 1 mg and 2 mg can also be filled at an alternative site with some available capacity, but this extra capacity cannot fully cover the main production line. This will result in intermittent shortages of NovoSeven 1 mg and 2 mg which are expected to last, at least throughout 2024.

Recommendation for Risk minimisation (in shortage situation)

- In case of emergency, physicians are advised to use another available strength of NovoSeven or an alternative bypassing agent.
- Use of suitable treatment alternatives to NovoSeven should only be initiated in consultation with a physician and requires strict medical supervision along with following requirements in the prescribing information.
- ***Alternative treatment options which can be considered*: *[to be updated by affiliate as relevant]:***

Important prescribing information in countries: Spain, Italy, Latvia, Lithuania, Czechia and Austria (usage of potentially under-filled vials)

- Novo Nordisk's medical evaluation and patient safety assessment of potential underfilling of some vials of NovoSeven 1 mg and 2 mg concluded that treatment with under-filled vials will still have therapeutic effect and the probability of serious adverse health consequences is very unlikely. Therefore, the vials can be used as indicated in the NovoSeven label.
- The likelihood of a patient receiving an under-filled vial is very low. This is due to extensive manual inspections during production, as a result of which, most under-filled vials were identified and removed before release.
- Based on NovoSeven product information, clinical assessment of response is necessary. When required, repeated dosing is recommended to achieve haemostasis as per the NovoSeven label.

Call for reporting

Adverse events including medication errors relating to NovoSeven should be reported to Novo Nordisk [contact details to be updated by affiliate] or to local authorities [to be modified according to national requirements].

Company contact point

Further information can be obtained by contacting <local Novo Nordisk affiliate contact details to be added by affiliate>

Yours Sincerely

Medical Director

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	NovoSeven® 1 mg and 2 mg (eptacog alfa)
Marketing authorisation holder(s)	Novo Nordisk A/S
Safety concern and purpose of the communication	Manufacturing issue leading to supply shortage. A manufacturing issue, combined with unrelated release delays from the packaging line and continued capacity constraints have aggravated the supply situation and it is expected to cause intermittent shortages at least throughout 2024 for NovoSeven® 1 mg and 2 mg.
DHPC recipients	Target group for this letter is general physicians and specialists that treat patients with haemophilia. Adding pharmacists or other health care providers to the recipients will be determined in agreement with the respective national competent authority.
Member States where the DHPC will be distributed	Dissemination of the DHPC will be determined in agreement with national competent authorities in individual Member States, as not all Member States may be impacted by supply shortages and only few Member States are impacted by the underfilled vial issue.

Timetable	Date
DHPC and communication plan (in English) agreed by CHMP	25 July 2024
Submission of translated DHPCs to the national competent authorities for review	05 August 2024
Agreement of translations by national competent authorities	12 August 2024
Dissemination of DHPC	19 August 2024