IMPORTANT DRUG WARNING

November 23, 2005

Dear Healthcare Professional,

Novo Nordisk is informing the medical community about the addition of new Warnings and Adverse Reactions to the labeling for NovoSeven® Coagulation Factor VIIa (Recombinant). This new information is based on data obtained from post marketing studies and routine safety surveillance.

The additional adverse events that have been added to the WARNINGS and ADVERSE REACTIONS sections of the labeling are based on clinical studies in non-hemophilia patients, and on post-marketing safety surveillance. The new information includes the following:

WARNINGS

The extent of the risk of thrombotic adverse events after treatment with NovoSeven in patients with hemophilia and inhibitors is not known, but is considered to be low. Patients with disseminated intravascular coagulation (DIC), advanced atherosclerotic disease, crush injury, septicemia, or concomitant treatment with aPCCs/PCCs (activated or nonactivated prothrombin complex concentrates) may have an increased risk of developing thrombotic events due to circulating TF or predisposing coagulopathy. (See **ADVERSE REACTIONS** and **Drug Interactions**)

The extent of the risk of arterial and venous thromboembolic adverse events after treatment with NovoSeven in patients without hemophilia is also not known. A clinical study in elderly non-hemophilia intracerebral hemorrhage patients indicated a potential increased risk of arterial thromboembolic adverse events with use of NovoSeven, including myocardial ischemia, myocardial infarction, cerebral ischemia and/or infarction.[11]

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ADVERSE REACTIONS

Postmarketing Experience

The following post marketing adverse events are reported voluntarily from a population of uncertain size; hence, it is not possible to estimate their frequency or establish a causal relationship to exposure.

The following additional adverse events were reported following the use of NovoSeven in both labeled indications and unlabeled indications that included individuals with situational coagulopathy and without known coagulopathy: high D-dimer levels and consumptive coagulopathy, thromboembolic events including myocardial infarction, myocardial ischemia, cerebral infarction and/or ischemia, thrombophlebitis, arterial thrombosis, deep vein thrombosis and related pulmonary embolism, and isolated cases of hypersensitivity reactions including anaphylactic reactions. (See **WARNINGS** and **PRECAUTIONS**)

Evaluation and interpretation of these post marketing events is confounded by underlying diagnoses, concomitant medications, pre-existing conditions, and inherent limitations of passive surveillance. A causal relationship has not been established for the above events.

Reference

11. Mayer SA, et al. Recombinant Activated Factor VII for Acute Intracerebral Hemorrhage. *New England Journal of Medicine.* 2005;352:777-785.

Thank you for taking time to review this letter, as well as the enclosed full Prescribing Information for NovoSeven. Should you have questions or require additional information, please call 1-877-NOVO-777.

Sincerely,

Michael Sumner, MD
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Novo Nordisk Inc.