To:
Head of Paediatric Medicines
European Medicines Agency
7 Westferry Circus
London E14 4HB
United Kingdom
paediatrics@ema.europa.eu

Notification of discontinuation of a paediatric development which is covered by an agreed PIP Decision

Actives substances(s): vatreptacog alfa (activated)
Invented name: Not applicale

Latest Decision number(s): 1) P/236/2011 2) P/ 3) P/ 4) P/

Corresponding PIP number(s): 1) EMEA-000328-PIP02-09 2) EMEA- 3) EMEA- 4) EMEA-

Please note that development of the medicinal product above in the [condition(s)/indication(s)]:
Treatment of hereditary factor VIII and factor IX deficiency

☒ has been discontinued
☐ has been suspended/put on long-term hold (with possible re-start at a later time)

for the following reason(s): *(tick all that apply)*

☐ (possible) lack of efficacy in adults
☐ (possible) lack of efficacy in children
☒ (possible) unsatisfactory safety profile in adults
☐ (possible) unsatisfactory safety profile in children
☐ commercial reasons (please specify:)
☐ manufacturing / quality problems
☐ other regulatory action (please specify:) *(e.g. suspension, revocation of M.A.)*
☐ other reason (please specify:)

Please add a brief description (max 2000 characters) of the reason(s) for the discontinuation / suspension:
On September 28 2012, Novo Nordisk announced the decision to discontinue the development of vatreptacog alfa. The decision followed analysis of the data from pivotal phase 3a trial adeptTM2. The trial demonstrated that both vatreptacog alfa and NovoSeven® could stop a 93% of bleeding episodes with three doses or less. However, eight patients developed anti-drug antibodies (ADA) to vatreptacog alfa, including one patient with a potentially neutralising effect in vitro in one sample. Four of these patients developed cross-binding antibodies to NovoSeven®. One patient developed a positive response for binding antibodies towards NovoSeven®just above cut-off point. None of the antibodies were inhibitory and patients responded well to treatment during the course of the trial. Similar anti-drug antibodies have not been reported for NovoSeven® when used for haemophilia patients with inhibitors to factor VIII and IX. Therefore, the observation of anti-drug antibodies and the potential risks thereof for haemophilia patients with inhibitors led Novo Nordisk to discontinue the development of vatreptacog alfa. All patients who developed ADA were offered participation in a follow-trial monitoring the ADA development. Eight patients, including two adolescent patients, agreed to participate. The level of ADA has declined in all patients; one of the adolescent patients is now ADA negative and no longer followed, while the other one still has a low titre ADA positive response. This patient will be followed until he is ADA negative, until he chooses to withdraw from the trial or until the investigator or Novo Nordisk judge further follow-up unnecessarry from a safety and scientific point of view. Novo Nordisk had planned to notify the PDCO about the termination of the project and the closure of the vatreptacog alfa PIP when both adolescent patients had complete

the follow-up trial. However, as this may take a very long time, we have decided to submit the notification now.

Name and signature of the PIP contact point:	Per Oestergaard
Date:	23 May 2014

Contact for inquiries from interested parties:	Please contact the email box described below
Telephone:	
Email:	paediatrics@novonordisk.com