The current version of this document has been redacted for immediate publication on the 08 March 2013.

The unredacted version of the document cannot be published at this stage as it contains data submitted "in confidence" by researchers to the EMA.

Under applicable EU law, a confidential treatment of these data has been granted for a limited period of time.

An updated, complete version of this notification is to be published at a later stage.

INITIATION OF THE PROCEDURE LAID DOWN IN ARTICLE 20 OF REGULATION (EC) No 726/2004

This is an initiation by the European Commission of a procedure under Article 20 of Regulation (EC) No 726/2004

Common name:	Recombinant coagulation factor VIII (octocog alfa)
Product Names:	Kogenate Bayer and Hexilate NexGen

Kogenate Bayer and Helixate NexGen contain the active substance human coagulation factor VIII (octocog alfa). The products were approved in the European Union on 04 August 2000 for the treatment and prevention of bleeding in patients with haemophilia A (an inherited bleeding disorder) and are intended for either short-term or long-term use.

Development of alloantibodies (inhibitors) against factor VIII (FVIII) is the most significant complication of replacement therapy for haemophilia. Antibodies inactivate the pro-coagulant activity of FVIII and inhibit patients' response to FVIII replacement therapy which may result in life-threatening bleedings and sequel.

An EMA expert meeting on FVIII products and inhibitor development held on 28 February to 2 March 2006 agreed by consensus that there was a need to collect comparable clinical data on the immunogenicity of recombinant and plasma-derived FVIII products as a long-term objective. As a consequence, the marketing authorisation holder (MAH) for Kogenate Bayer and Helixate NexGen supported two EU registries – EUHASS (European Haemophilia Safety Surveillance System registry) and RODIN. Both registries are part of the risk management plan (RMP) for Kogenate Bayer and Helixate NexGen and therefore part of the pharmacovigilance activities of the MAH.

The results of the RODIN/PedNet registry have recently been published ([1]).which showed that second-generation full-length products (Kogenate Bayer, Helixate NexGen) were associated with an increased risk of inhibitor development as compared with third generation full-length recombinant products.

[redacted]

In light of the current emerging data resulting from pharmacovigilance activities, which may suggest new risks or changed risks, the Federal Institute for Vaccines and Biomedicines (Germany) informed the Commission services on 1st March 2013 that there is a need to review the impact of these results on the benefit-risk balance of Kogenate Bayer and Helixate NexGen.

Therefore, the European Commission (EC) initiates a procedure under Article 20 of Regulation (EC) No 726/2004 and requests the Agency to assess the data provided by Germany and its impact on the benefit-risk balance of the medicinal products concerned and to give its opinion as to whether measures are necessary to ensure the safe and effective use of these products and specifically on whether the marketing authorisations should be maintained, varied, suspended or withdrawn. As the request results from the evaluation of data resulting from pharmacovigilance activities, the procedural steps of Article 31 of Directive 2001/83/EC should be applied as referred to in Article 20(8) of Regulation (EC) No 726/2004.

[redacted]

[Signed]
Sabine Jülicher
Head of Unit Medicinal Products-authorisations, EMA
Health and Consumers DG

[1] Gouw S et al: Factor VIII products and inhibitor development in severe Hemophilia A, N Engl J Med 2013;368:231-9