07 March 2013
EMA/PRAC/142800/2013

PRAC List of questions

To be addressed by the marketing authorisation holder for Kogenate Bayer and Helixate NexGen

Procedure under Article 20(8) of Regulation (EC) No 726/2004, following procedural steps of Article 31 resulting from pharmacovigilance data

Procedure numbers: Kogenate Bayer EMEA/H/C/000275/A-20/0150
Helixate NexGen EMEA/H/C/000276/A-20/0143

INN/ active substance: octocog alfa

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The marketing authorisation holder MAH for Kogenate Bayer and Helixate NexGen is requested to:

Question 1

An analysis of low and high titre inhibitor development in previously untreated patients (PUPs) from (I) all clinical trials and (II) observational studies conducted by the MAH as well as by independent investigators should be provided.

The analysis should consider:

a) The frequency of inhibitor development per patient and per exposure days
b) The method of inhibitor detection
c) The frequency of inhibitor testing
d) The length of follow-up in terms of exposure days
e) Known risk factors of patients included in clinical trials such as severity of haemophilia A (number of patients with Factor VIII activity <1 % and < 2 %), major FVIII gene defects, family history and non-Caucasian race, age at first treatment, intensity of early treatment and use of prophylaxis.
f) Bleeding episodes and clinical outcome associated with inhibitor development
g) The MAH should discuss possible bias of studies (e.g. enrolment bias, centre effects)

Question 2

The MAH should analyse head to head comparisons with other recombinant Factor VIII products.

Question 3

The MAH should provide reporting rates of inhibitor development in PUPs based on number of PUPs treated for Kogenate Bayer/ HelixateNexGen.

Question 4

The MAH is requested to provide data on mechanistic studies of functional antibodies inhibiting octacog alfa (e.g. impact of glycosylation of Kogenate Bayer on antibody development).

Question 5

The MAH is requested to provide a full risk benefit analysis for Kogenate Bayer/ HelixateNexGen for PUPs taking into account the clinical relevance of inhibitor development.

Question 6

a) Please provide details of any specific measures that have already been taken in order to minimise the risk of inhibitor development in patients using Kogenate Bayer and Helixate NexGen and comment on the impact of such measures.

b) Please provide proposals and justification with supportive evidence for any risk minimisation measures to address the risk of inhibitor development in patients using Kogenate Bayer and Helixate NexGen, including changes to the Summary of Product Characteristics, Labelling and Package Leaflet, which could be taken in order to improve the benefit/risk of Kogenate Bayer and Helixate NexGen. Please also comment on how the impact of such measures should be monitored and assessed.