HAUTE AUTORITÉ DE SANTÉ

HAEMATOLOGY
Focus
July 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

HELIXATE NexGen and KOGENATE Bayer

(octocog alfa), recombinant human coagulation factor VIII

In previously untreated patients with a severe haemophilia A, last-line treatment to be used in case of a functional or life-threatening emergency and in the absence of the other available FVIII.

Main points

- HELIXATE NexGen and KOGENATE Bayer, identical medicinal products, have Marketing Authorisation in the treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency).
- The efficacy of replacement therapy for haemophilia A using FVIII concentrates may be compromised by the development of inhibitors of FVIII activity, the most serious complication of the treatment.
- KOGENATE Bayer/HELIXATE NexGen is likely to increase the risk of inhibitors development compared to other recombinant FVIII in patients with severe, previously untreated, haemophilia A.

Therapeutic use

- The aim of therapeutic management of haemophilia A is early control and/or to prevent bleeding episodes and their short and long-term complications. This global management should be adapted to each patient, based on the clinical and laboratory context, by physicians with experience in bleeding disorders.
- The first-line treatment for haemophilia A is replacement therapy involving the administration of coagulation factor VIII concentrates. According to the guidelines, these can be administered:
  - as curative treatment ("on demand" treatment) upon occurrence of uncontrolled bleeding event by local haemostatic measures or not suitable for treatment with desmopressin or tranexamic acid ;
  - in bleeding prevention: as primary prophylaxis in children with severe haemophilia aged under 2 years and before the occurrence of a second haemarthrosis, as secondary prophylaxis (long-term or intermittent) after the occurrence of a second haemarthrosis, or during surgery or invasive procedures (depending on the severity and the risk of bleeding expected).

Role of the medicinal product in the therapeutic strategy

Given the clinical data currently available, these proprietary medicinal products are:

- first-line treatments in patients with haemophilia A (having accumulated at least 75 days of treatment), regardless of the severity of the haemophilia, and in previously untreated patients (PUPs) with a mild or moderate form of haemophilia;
- last-line treatments in patients with severe, previously untreated, haemophilia A. In this case, these proprietary medicinal products should be used in case of functional or life-threatening emergencys and in the absence of the other available FVIII.

Clinical data

- Several observational studies have been conudcted to evaluate the risk of inhibitors development in previously untreated patients (PUPs) with severe form of haemophilia A, population most at risk.
- A study published in 2013 suggested for the first time that there was a higher risk of the development of inhibitors with KOGENATE Bayer/HELIXATE NexGen than with ADVATE (third-generation recombinant FVIII) in this population. The EMA re-evaluated these drugs and, after analysis of the available data, concluded, at the end of 2013, with the lack of difference in risk.

- Since the results of three new observational studies from national cohorts (French registry the FranceCoag network, British Haemophilia Database, Canadian cohort) were published, as a study relating to the data in the European pharmacovigilance registry EUHASS.
- Only the study based on the British cohort produced statistically significant evidence of an increased incidence of inhibitors with KOGENATE Bayer/HELIXATE NexGen compared with ADVATE, although in all cases the results were less favourable for KOGENATE NexGen/HELIXATE Bayer.
- However, several limitations to interpret these results can be raised. The impact of the various biases on their results cannot be quantified. It therefore appears difficult to conclude to an association between use of factor VIII products KOGENATE Bayer/HELIXATE NexGen and an increase in the risk of inhibitors development compared with other recombinant FVIII in patients with previously untreated haemophilia A. Nevertheless, an association cannot be completely ruled out.

Special prescribing conditions

- Medicine requiring initial hospital prescription for 6 months.

Benefit of the medicinal product

- The actual benefit* of HELIXATE NexGen and KOGENATE Bayer remains substantial.
- Recommends continued inclusion on the list of reimbursable products for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 01 July 2015 (CT-13917 and CT-13580) and is available at **www.has-sante.fr**

[i] * The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means "no clinical added value".