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PRAC considers benefits of Kogenate Bayer/Helixate NexGen outweigh risks in previously untreated patients

Current evidence does not confirm increased risk of inhibitor development compared with other factor VIII products

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has reviewed the medicines Kogenate Bayer and Helixate NexGen and concluded that current evidence did not confirm an increased risk of developing antibodies (factor VIII inhibitors) against these medicines when compared with other factor VIII products in previously untreated patients with the bleeding disorder haemophilia A. Therefore, the benefits from taking Kogenate Bayer and Helixate NexGen, which are known as second generation factor VIII products, continue to outweigh the risks. Factor VIII is needed for blood to clot normally and is lacking in patients with haemophilia A.

The review of the PRAC followed results from the RODIN study[1], as well as preliminary 3-year data from the European haemophilia safety and surveillance system (EUHASS). The RODIN study looked at data from 574 previously untreated children with haemophilia A who were given different factor VIII products. About a third (177) of all the children developed factor VIII inhibitors against their medicine, which reduces the benefit and makes bleeding more likely. This is a known risk of all factor VIII products but the authors of the study concluded that children given so-called second generation full-length recombinant factor VIII products such as Kogenate Bayer or Helixate NexGen were more likely to develop antibodies than those given a third generation recombinant product. An increase in inhibitor formation was not seen with other recombinant or plasma-derived factor VIII products.

The PRAC reviewed available scientific and clinical data on development of inhibitors in previously untreated patients, including from RODIN and EUHASS, and concluded that the available data did not support that Kogenate Bayer or Helixate NexGen were associated with an increased risk of developing factor VIII inhibitors compared with other products. Although the existing risk minimisation measures were considered adequate for both Kogenate Bayer and Helixate NexGen and should be continued, the PRAC recommended that the product information should be updated with results from the RODIN study.

The PRAC recommendation will now be forwarded to the Committee on Human Medicinal Products (CHMP), which will adopt a final opinion at its plenary meeting of 16-19 December 2013.

[1] Gouw SC, et al; PedNet and RODIN Study Group. Factor VIII products and inhibitor development in severe hemophilia A. N Engl J Med 2013; 368: 231-9.

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More about the medicine

Kogenate Bayer and Helixate NexGen are identical medicines that were authorised throughout the European Union (EU) on 4 August 2000. The marketing authorisation holder for both medicines is the same company, Bayer Pharma AG.

Kogenate Bayer and Helixate NexGen are known as second generation factor VIII products. They contain a form of factor VIII, octocog alfa, produced by a method known as 'recombinant DNA technology': it is made by cells into which a gene (DNA) has been introduced which makes them able to produce the clotting factor. The octocog alfa in these products has the same structure as natural factor VIII ('full-length'). They are used to replace the factor VIII that is lacking in patients with haemophilia A, an inherited bleeding disorder. Untreated, the deficiency of factor VIII in these patients causes bleeding problems, including bleeding into joints, muscles, and internal organs that can lead to severe damage.

Alternative products containing various forms of factor VIII are available and may be used similarly. These may be extracted from human blood ('plasma-derived'), produced as full-length recombinant products with varying degrees of exposure to other blood-derived proteins (first, second, or third generation), or may contain a shortened, but still active, recombinant form of the factor VIII molecule.

More about the procedure

The review of Kogenate Bayer and Helixate NexGen was initiated on 05 March 2013 at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004, and follows the procedural steps laid out in Article 31 of Directive 2001/83.

The review has been carried out by the PRAC, the committee responsible for the evaluation of safety issues for human medicines, which has made a set of recommendations. The PRAC recommendations will now be forwarded to the CHMP, the committee responsible for all questions concerning medicines for human use, which will adopt a final opinion. This will then be sent to the European Commission for a final legally binding decision throughout the EU.