The European Agency for the Evaluation of Medicinal Products
*Post-authorisation evaluation of medicines for human use*

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**EMEA PUBLIC STATEMENT ON BENEFIX (nonacog alfa)**

**- INTENSIVE POST-MARKETING SURVEILLANCE FOR ALL NEW PATIENTS –**
**- NEW CLINICAL TRIALS –**

**The European Medicines Evaluation Agency's (EMEA) scientific committee for human medicines, the Committee for Proprietary Medicinal Products (CPMP), has recommended intensive post-marketing surveillance for all new patients treated with BeneFIX (nonacog alfa, human recombinant factor IX) as well as the initiation of two new clinical studies.**

The CPMP have made this recommendation because a Good Clinical Practice (GCP) **inspection of two of the three pivotal clinical studies, on which the Marketing Authorisation for BeneFIX is based, revealed deficiencies which cast doubts on the reliability of the clinical data.** An independent audit of the three clinical studies, commissioned by Genetics Institute, confirmed the GCP deficiencies, but found the data to be representative of the patient population studied.

BeneFIX has been commercially available in the United States since 1997 and in Europe since 1999. Post-marketing data accumulated since then from physicians treating haemophilia B patients support the safety and efficacy profile of BeneFIX. **The CPMP considers that the benefit/risk balance of BeneFIX for the treatment and prophylaxis of bleeding in previously treated patients (PTPs) with haemophilia B is positive, based on the data presently available.** However, the data are insufficient to be certain of the frequency of some adverse drug reactions, especially those linked to inhibitor formation and to allergic reactions. In view of this, there is a need for enhanced surveillance of new patients receiving BeneFIX.

**This intensive post-marketing surveillance will include a registry for ALL NEW PATIENTS treated with BeneFIX in Europe.** The Marketing Authorisation Holder is currently working with the CPMP on the design of this registry. In the meantime, new patients may start treatment with BeneFIX with careful monitoring for adverse drug reactions.

**Patients already treated with BeneFIX may continue their therapy.** However, patients who experience suspected adverse drug reactions should be monitored carefully and the risk/benefit of continued treatment should be evaluated.

All suspected adverse drug reactions should be reported to the Marketing Authorisation Holder or National Health Authorities.

In the case of severe allergic reactions, alternative haemostatic measures should be considered.

In addition to the present recommendation to check for the presence of inhibitor when a lack of efficacy is observed at the recommended dose, a new recommendation will be implemented to switch patients to another factor IX product if doses higher than 100 IU/kg have been repeatedly needed during routine prophylaxis or treatment, even if an inhibitor is not detected.

**With regard to the treatment of children with BeneFIX**, it is known that children may respond differently to FIX than adults. To date, there are insufficient data to recommend the use of BeneFIX in children less than 6 years of age.
Furthermore, there are insufficient data to provide information on inhibitor incidence in previously untreated patients (PUPs).


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**At the request of the CPMP, two new clinical trials will be conducted** to collect new efficacy and safety data on the product. The scope of these trials will be as follows:

- The use of BeneFIX in 20 previously treated patients
- The use of BeneFIX in at least 20 children less than 6 years of age, including previously treated patients and previously untreated patients

These trials will be conducted in accordance with the Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and the recent CPMP Note for Guidance on the Clinical Investigation of Recombinant Factor VIII and IX products (CPMP/BPWG/1561/99).

These trials will generate reliable data on the use of BeneFIX in PTPs and, in addition, will investigate whether BeneFIX can be recommended for use in children less than 6 years of age and PUPs.

Genetics Institute of Europe BV, the Marketing Authorisation holder of BeneFIX, is in the process of implementing corrective actions to address the deficiencies found in the GCP inspection.

The EMEA thought it necessary to provide this new information to the public. Furthermore, the MAH has brought it to the attention of prescribing physicians. The Summary of Product Characteristics and Package Leaflet have been updated in line with this information and can be found in the European Public Assessment Report for BeneFIX on the EMEA website.

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