The European Agency for the Evaluation of Medicinal Products
*Evaluation of Medicines for Human Use*

**CPMP/2337/03**

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# EMEA PUBLIC STATEMENT ON REFACTO (moroctocog alfa)

## INTRODUCTION OF A CHANGE TO REFACTO DRUG PRODUCT SPECIFIC ACTIVITY SPECIFICATION INCREASE OF 20% IN THE AMOUNT OF REFACTO PROTEIN IN EACH VIAL

On 8 May 2003, the European Commission issued an authorisation valid throughout the European Union to vary the current marketing authorisation for ReFacto.
This decision is based on the MAH's scientific data provided in support of the variation assessment report and on the favourable opinion adopted by the scientific Committee for Proprietary Medicinal Products (CPMP).
Following approval by the European Commission, the EMEA within its Scientific Committee (CPMP) decided to make the following information public:

Wyeth will shortly implement a change in ReFacto manufactured using a new reference standard of calibration of specific activity. This change will result in an increase of the amount of ReFacto protein in each vial by approximately 20%, however the marketed ReFacto labelled dosage strength (250, 500, 1000 and 2000 IU/vial) remains unchanged. Wyeth intends to introduce this change in early July 2003. It is anticipated that haemophilia centres as well as hospital pharmacies in connection with haemophilia centres would switch their existing ReFacto inventory to new ReFacto by September 2003.

ReFacto is indicated for the treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency). ReFacto does not contain von Willebrand factor and hence is not indicated in von Willebrand's disease.

Revised Standard Used to Assign ReFacto Potency
A recent collaborative study conducted by a number of European Official Medicinal Control Laboratories (OMCLs) demonstrated variability among laboratories in the potency assessment of ReFacto using chromogenic substrate assays. With the approval of the European regulatory authorities, Wyeth has recalibrated the standard used to establish the amount of protein per international unit of the ReFacto drug product.
As a result, the assigned potency of the current ReFacto reference standard is approximately 20% higher than the value obtained from the recent collaborative study. Using this new potency value, the specific activity is recalculated as 11,000 IU/mg protein instead of the previous 13,000 IU/mg protein. Therefore, the Summary of Product Characteristics has been updated to reflect the newly assigned specific activity.

**The EMEA wishes to highlight the following important safety information:**

**For physicians treating patients with ReFacto:**

- This change will be associated with distinctive **new packaging** which will be easily identified by new, distinctly different 'colour-coordinated' packaging.
- At present, **patients** should continue with their current supply of ReFacto.



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- Once **patients** are switched to ReFacto's new "colour-coordinated" packaging, it is recommended that patients continue to use only ReFacto's new "colour" packaging. If patients have any questions, they should consult their prescribing physician or Haemophilia Treatment centre.

- **Patients** switching to the new batches should initially use the same dose of ReFacto as previously prescribed. Following the transition, as recommended in the Summary of Product Characteristics*, "doses administered should be titrated to the patients' clinical response. During the course of treatment, appropriate determination of factor VIII levels is advised to guide the dose to be administered and the frequency of repeated infusions."*[1]

- Finally, the introduction of this change will also be associated with the **availability** of an updated ReFacto Laboratory Standard™.

- **<u>Updated ReFacto Laboratory Standard</u>**

When monitoring patients' factor VIII activity levels during treatment, the preferred method remains the chromogenic substrate assay. It is strongly recommended that this method be used instead of the one-stage clotting assay if possible.[1]
To minimise the discrepancy between results obtained with the one-stage clotting assay and those obtained with the chromogenic substrate assay, the ReFacto Laboratory Standard™ has been developed. Wyeth will provide an updated version of the ReFacto Laboratory Standard ™, free of charge, to clinical laboratories using the standard, approximately one month prior to the release of the new ReFacto batches. Laboratories should discard the old laboratory standard upon receipt of the new ReFacto Laboratory Standard™.

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[1]ReFacto Summary of Product Characteristics