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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

CONCEPT PAPER ON THE REVISION OF NOTES FOR GUIDANCE ON THE CLINICAL INVESTIGATION OF HUMAN PLASMA DERIVED AND RECOMBINANT FACTOR VIII AND IX PRODUCTS AND THE CORRESPONDING CORE SPCs

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CONCEPT PAPER ON THE REVISION OF COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP) GUIDELINES ON

CLINICAL INVESTIGATION OF HUMAN PLASMA DERIVED AND RECOMBINANT FACTOR VIII AND IX PRODUCTS AND THE CORRESPONDING CORE SPCS

1. Introduction and problem statement

The current Guideline on the Clinical Investigation of Human Plasma Derived Factor VIII and IX products (CPMP/BPWG/198/95 Rev. 1, Adopted Oct. 2000) and the Guideline on the Clinical Investigation of Recombinant Factor VIII and IX products (CPMP/BPWG/1561/99) have been in operation since October 2000 and the corresponding current core SPCs (CPMP/BPWG/1619/99 and CPMP/BPWG/1625/99) were approved in June 2000. In light of the increasing medical knowledge and the regulatory experience within this area a review of these guidance documents appears appropriate.

As examples the following aspects are proposed to be considered:

- The recommended pharmacokinetic characterisation of a new or modified product including frequency of blood sampling necessary and parameters to be followed and the assay methods used.
- An update is needed regarding the current methods in use for the reduction of the risk for transmissible diseases from plasma derived medicinal products and the corresponding texts in the core SPCs taking the recently revised regulatory guidelines within this area into account.
- The design of the clinical studies needed to support regulatory approval for treatment of children. Particular attention will be given to the number of patients available, the differing responses between children and adults and safety issues, e.g. inhibitor formation and pharmacokinetic data.
- The clinical evaluation of continuous infusion as well as the corresponding appropriate wording of the posology. The possible advantages of this mode of administration (e.g. reduced consumption) as well as the possible disadvantages (e.g. increased risk for inhibitor development) need to be addressed.
- The need for a prospective risk management plan for the post-marketing follow-up of new products with regard to the risk for inhibitor development should be taken into account.
- It should be determined if, in the dosing recommendations, the coagulation factor levels should be expressed in terms of IU/dL as previously, or in IU/mL, or possibly in KIU/L.
- Updated guidance on the evaluation and use of these products in patients with inhibitors, particularly the induction of immune tolerance.

2. Discussion and recommendation

It is proposed that the current Guidelines and core SPCs for plasma derived and recombinant factor VIII and IX products are updated in line with the above.

3. Timetable and resource requirements for preparation

It is anticipated that a draft revision of the documents will be available for a final discussion at the Blood Products Working Group within 9 months after the adoption of the Concept Paper by the CHMP.

4. Involvement of external parties

Interested parties with specific interest in this topic will be consulted during the revision of these guidelines, including [1]EPFA, PPTA, EHC and ISTH.

5. Impact assessment

The revised Guidelines will reflect the increasing medical knowledge and the regulatory experience within the area of hemophilia A and B. It will result in a more consistent assessment of applications for clinical trials and of postmarketing surveillance by regulators, set clear standards and expectations for industry, and therefore be helpful in a harmonised regulatory policy.

The relatively small resource implications for revision of the Guidelines are fully justified and are compensated by the fact that application of a Guideline will make assessment easier and will result in less resources being needed during assessment.

[1] EPFA: European Plasma Fractionation Association
PPTA: Plasma Protein Therapeutics Association
EHC: European Haemophilia Consortium
ISTH: The International Society on Thrombosis and Haemostasis