The European Agency for the Evaluation of Medicinal Products
Human Medicines Evaluation Unit

CPMP/1493/01

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS (CPMP)

SUMMARY INFORMATION ON A REFERRAL OPINION FOLLOWING AN ARBITRATION

PURSUANT TO ARTICLE 11 OF COUNCIL DIRECTIVE 75/319/EEC AS AMENDED, FOR

Engerix B

Common Name: recombinant hepatitis B vaccine

BACKGROUND INFORMATION

The active substance of Engerix B is a purified recombinant hepatitis B surface antigen, which is a non-infectious substance that protects adults and infants from hepatitis B by stimulating an immune response (immunogenic activity) against these diseases. There are two strengths of Engerix B 10 and 20 µg.The 20 µg dose (in 1.0 ml suspension) is intended for use in adults and children older than 15 years of age whereas the 10 µg dose (in 0.5-ml suspension) is intended for use in children up to and including 15 years of age, including neonates. The two strengths 10 and 20 µg are registered in all Member States of the European Union, except in the Netherlands where only the 20 µg strength is available.

National licenses were originally granted to the company SmithKline Beecham, for Engerix B vaccine in all 15 EU Member States. From these registrations and the subsequent variations, different Summaries of Product Characteristics (SPC) have been issued, based on national, divergent decisions. The differences in the SPC text relate to several sections: Therapeutic indication, Posology and method of administration, Special warning and special precautions for use, Interactions, Undesirable effects, Pharmacodynamic properties and List of excipients of the SPC.

On 7 October 1999, SmithKline Beecham Biologicals S.A acting on behalf of the all Marketing Authorisation Holders of each Member State presented to the EMEA a referral under Article 11 of Council Directive 75/319/EEC as amended, in order to harmonise the Summaries of Product Characteristics within the Member States. A proposal of Summary of Product Characteristics based on an updated dossier was provided.

The referral procedure started on 22 October 1999. The basis for this arbitration procedure was a harmonisation of the Summaries of Product Characteristics. The CPMP having considered the Rapporteur and the Co-Rapporteur assessment reports, Scientific discussion within the Committee and comments from the Marketing Authorisation Holders, was of the opinion that the benefit/risk ratio of Engerix B is favourable for the agreed indications and the above mentioned sections of the SPC. The CPMP issued a positive opinion, on 13 April 2000, recommending the harmonisation of the Summaries of Product Characteristics for Engerix B.

An overall summary of the scientific evaluation is provided, together with the amended Summaries of Product Characteristics.

A Decision was issued by the European Commission on 28 August 2000.

7 Westferry Circus, Canary Wharf, London E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 85 45
E-mail: mail@emea.eudra.org http://www.emea.eu.int/

SCIENTIFIC CONCLUSIONS

Overall summary of the scientific evaluation of Engerix B

The indication of the Hepatitis B vaccine is clearly for the prevention of hepatitis B infection and the target population is the global population. It is a matter of political strategy to define priorities and populations at risk for the transient implementation period of the vaccine worldwide. These priorities are not integral part of the indication. Therefore it was agreed that the categories within the population to be immunised should be determined on the basis of official recommendations, and is stated as such in the harmonised Summaries of Product Characteristics (SPC).

The different schedules proposed appear to be acceptable. However only one of them can be used as a standard schedule. The matter of doses is also a cost-benefit / risk-benefit assessment. Three doses given at times 0, 1, 6 seem the best compromise, with a cut-off age for the 10 µg (switching thereafter to 20 µg) at 15 years.

Concerning the booster dose, it was agreed that the need for a booster dose in healthy individuals should be determined according to official vaccination programs. However for immuno-compromised vaccinees (namely e.g. haemodialysis patients, HIV infected subjects) the recommendation was that a booster dose may be considered on a case-by-case basis in order to ensure a protective antibody level of > 10IU/ml..

Based on the clarification provided by the company that vaccination with either plasma-derived or recombinant hepatitis B vaccines prevents the transmission of HBV infection, the SPC was modified accordingly replacing “plasma-derived hepatitis B vaccine” with “hepatitis B vaccination”.

Two additional side-effects have been reported following a PSUR that dealt with more than 350 million doses of Engerix B, over a 5 year period up to June 30, 1999. In this context, thrombocytopenia and convulsions have been appropriately included in the SPC.

The wording proposed by the Pharmacovigilance Working Party (EMEA/CPMP/PHVWP/2033/99) in the Thiomersal Warning Statement Relating to Sensitisation was included in the harmonised SPC, excluding the changes proposed by the company.

Benefit/Risk considerations

The CPMP, having considered responses provided by the company as set out in the variation assessment report, is of the opinion that the harmonisation of the SPC as proposed by the company and including the amendments as discussed by the CPMP should be accepted.

GROUNDS FOR AMENDMENT OF THE SUMMARIES OF PRODUCT CHARACTERISTICS

Whereas,

- the scope of the referral was the harmonisation of the Summaries of Products Characteristics,
- the Summary of Products Characteristic proposed by the Marketing Authorisation Holders has been assessed based on the documentation submitted and the scientific discussion within the Committee,

the CPMP has recommended the amendment of the Marketing Authorisations for which the Summaries of Product Characteristics are attached.