EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Infanrix penta

(Diphtheria (D), Tetanus (T), Pertussis (Acellular, Component) (Pa), Hepatitis B (Rdna) (Hbv), Poliomyelitis (Inactivated) (Ipv) Vaccine (Adsorbed))

Procedure No. EMEA/H/C/P45/047

CHMP assessment report for paediatric use studies submitted according to Article 45 of the Regulation (EC) No 1901/2006

Assessment Report as adopted by the CHMP with all information of a commercially confidential nature deleted

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1. INTRODUCTION

GSK Biologicals' diphteria-tetanus-acellular pertussis, hepatitis B, and inactivated polio (DTPa-HBV-IPV) vaccine, Infanrix penta, was licensed, via the centralised procedure, in the European Union on 23rd October, 2000. In the USA, the vaccine is registered under the tradename "Pediarix". The DTPa-HBV-IPV vaccine is now licensed in 35 countries and nearly 42.5 million doses have been distributed since launch of the vaccine.

Infanrix penta is indicated for primary and booster vaccination of infants against diphteria, tetanus, pertussis, hepatitis B and poliomyelitis.

All clinical studies regarding Infanrix penta submitted up to 01/2010 in the context of the Article 45 of the pediatric regulation have been reviewed during the renewal procedure Infanrix penta EMEA/H/C/000295/R/0067.

2. SCIENTIFIC DISCUSSION

2.1. Clinical study

One clinical study (DTPa-HBV-IPV-020) evaluating Infanrix penta has been submitted to the CHMP in the context of Article 45 of the pediatric regulation. This study evaluated Infanrix penta administered as a booster dose given to infants in the second year of life, when co-administered with Haemophilus influenzae type b (Hib) conjugate vaccine Hiberix or with unconjugated Hib polysaccharide PRP, following priming with Infanrix penta/Hiberix in primary vaccination study DTPa-HBV-IPV-007.

In booster vaccination study DTPa-HBV-IPV-020, Infanrix penta was administered as a booster vaccine following priming with Infanrix penta mixed with Hiberix vaccine in primary vaccination study DTPa-HBV-IPV-007. A total of 48 subjects received a fourth dose of Infanrix penta at the age of 16 to 22 months, either co-administered with Hiberix or with unconjugated Hib polysaccharide PRP.

In this trial, only the antibody response to the Hib polysaccharide PRP was assessed. Blood samples were taken prior the administration of the booster dose to evaluate the antibody persistence against PRP induced by the primary vaccination course.

The frequency and severity of the adverse events reported after booster vaccination in DTPa-HBV-IPV-020 were similar to those listed in the current SPC of Infanrix penta.

One subject receiving a booster dose of Infanrix penta co-administered with unconjugated PRP reported a SAE (hyperthermia 40°C) that was considered as possibly related to the vaccine by the investigator.

The immune response against PRP after booster vaccination with Infanrix penta observed in this study was not different from what was initially reported.

2.2. Post-marketing surveillance study

The final report of a large post marketing surveillance (PMS) study conducted in the USA (study DTPa-HBV-IPV-088) including 61.004 infants who received Infanrix penta co-administered with Prevenar has become available since initial renewal in 2005. The study has been submitted to the CHMP in the context of Article 45 of the paediatric regulation.

This study was conducted in families covered by the Southern California Kaiser Permanente Health Care Plan, corresponding to a birth cohort of approximately 30.000 to 35.000 infants per year.

The study, which was to analyse data from a complete three-dose primary course of vaccination in 40.000 infants, had two primary objectives:

The evaluation of the incidence of seizures (with and without fever) during the first 8-day period after vaccination

The evaluation of the frequency of medically-attended fever during the first 4-day period after vaccination.

Secondary objectives included evaluation of the incidence of allergic reactions, outpatient visits for any cause, hospitalisations for any cause and deaths.

The incidences of these events were to be compared with data from a historical cohort of age-, gender-, and area-matched infants who had received DTPa vaccine.

Safety was evaluated in a total of 61.004 infants who received Infanrix penta co-administered with Prevnar compared to a Historical control of 58.251 age, gender and area-matched infants who received a DTPa vaccine other than Infanrix penta co-administered with Prevnar. For the 61.004 subjects in the Infanrix penta cohort, 18.231 (29.9%) of the subjects received one dose of Infanrix penta and 42.773 (70.1%) of the subjects received 2 or more doses, with data collected for 40.000 subjects/dose.

In terms of co-primary objectives, there does not appear to be an increased likelihood of either seizures or medically-attended fever in the cohort which received Infanrix penta with respect to historical controls.

Based on this large, post-licensure study it can be concluded that the occurrence of clinically-relevant events such as medically-attended fever, seizures with or without fever, allergic reactions, outpatient visits for any cause, hospitalisations for any cause and deaths are comparable in infants receiving the combination vaccine Infanrix penta relative to a similarly sized group receiving DTPa vaccine.

3. Rapporteur's Overall Conclusion and recommendation

No new efficacy or safety data emerged that alter the benefit risk balance of Infanrix penta. The data provided are in line with what was previously reported with Infanrix penta. Therefore, no changes to the SmPC or PIL are necessary and no other regulatory action is required.

The Rapporteur is of the opinion that the Article 45 procedure for Infanrix penta can now be considered closed.