25 April 2013
EMA/359928/2014
Committee for Medicinal Products for Human Use (CHMP)

Assessment report under Article 46

Infanrix hexa

International non-proprietary name: diphtheria (d), tetanus (t), pertussis (acellular, component) (pa), hepatitis b (rdna) (hbv), poliomyelitis (inactivated) (ipv) and haemophilus influenzae type b (hib) conjugate vaccine (adsorbed)

Procedure No. EMEA/H/C/000296/P46/106.1

Note

Variation assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

ADMINISTRATIVE INFORMATION

Invented name of the medicinal product:	Infanrix Hexa
INN (or common name) of the active substance(s):	Diphtheria toxoid, adsorbed/ Tetanus toxoid, adsorbed/ Pertussis toxoid, adsorbed/ Filamentous haemagglutinin, adsorbed/ Pertactin, adsorbed/ Recombinant Hepatitis B surface Antigen (S protein), adsorbed/ Inactivated type 1 Poliovirus/ Inactivated type 2 Poliovirus/ Inactivated type 3 Poliovirus/ Conjugate of Haemophilus influenzae type b capsular polysaccharide and Tetanus toxoid, adsorbed
MAH:	GSK Biologicals (GlaxoSmithKline Biologicals) S.A.-N.V.(Belgium)
Currently approved Indication(s)	Infanrix hexa is indicated for primary and booster vaccination of infants against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and disease caused by *Haemophilus influenzae* type b.
Pharmaco-therapeutic group (ATC Code):	J07CA09 - Diphtheria-hemophilus influenzae B-pertussis-poliomyelitis-tetanus-hepatitis B
Pharmaceutical form(s) and strength(s):	Powder and suspension for suspension for injection in a pre-filled syringe After reconstitution, 1 dose (0.5 ml) contains: Diphtheria toxoid not less than 30 International Units (IU) Tetanus toxoid not less than 40 International Units (IU) *Bordetella pertussis* antigens Pertussis toxoid ** 25 micrograms Filamentous Haemagglutinin ** 25 micrograms Pertactin ** 8 micrograms Hepatitis B surface antigen ** 10 micrograms Poliovirus (inactivated) type 1 (Mahoney strain) ** 40 D-antigen unit type 2 (MEF-1 strain) ** 8 D-antigen unit type 3 (Saukett strain) ** 32 D-antigen unit *Haemophilus influenzae* type b polysaccharide (10 micrograms) (polyribosylribitol phosphate) conjugated to tetanus toxoid as carrier protein approximately 25 microgram

1. Executive Summary

This document contains the assessment of the first round responses by the MAH.

No SmPC and PL changes are proposed.

2. Rapporteur's Overall Conclusion AND RECOMMENDATION

The MAH submitted the results of a double-blind, randomised, multicentre study to assess safety and immunogenicity of 2 new formulations of the MAH's DTPa-HBV-IPV/Hib vaccine compared to the licensed Infanrix Hexa vaccine when co-administered with Prevenar 13 to healthy infants as a primary vaccination course at 2, 3 and 4 months of age.

The primary objective, i.e. non-inferiority of the immunogenicity of at least one of the novel DTPa-HBV-IPV/Hib vaccine formulations compared to the licensed Infanrix Hexa vaccine, was not met according to the criteria set for non-inferiority, as the immune response to the pertactin component of both novel formulations was not non-inferior to Infanrix Hexa. No divergent safety signals were detected in the comparison of the new formulation with the licensed Infanrix Hexa.

The MAH should continue to investigate in pertussis vaccines that offer prolonged protection compared to the currently authorised vaccines in view of the resurgence of pertussis in fully vaccinated individuals which appears to be at least partly due to waning vaccine-induced immunity (Cherry, 2012).

A request for supplementary information was provided to the MAH, who is at current not able to submit a sufficiently detailed answer. A full report will be submitted by the MAH once all relevant data have been captured.

No changes in the SmPC are warranted.

3. Request for supplementary information

Request for supplementary information: In view of failure to show non-inferiority for both new formulations against the approved formulation in relation to immunogenicity, the applicant should clarify backup development strategy and consequential deliverables.

Reference

Cherry, J. D. (2012). Epidemic Pertussis in 2012 — The Resurgence of a Vaccine-Preventable Disease. New England Journal of Medicine, 120815140022001. doi:10.1056/NEJMp1209051

4. MAH's RESponses to the RSI

Question No. 1 - Regulatory

In view of failure to show non-inferiority for both new formulations against the approved formulation in relation to immunogenicity, the applicant should clarify backup development strategy and consequential deliverables.

Company's answer: The Company has put on hold any further clinical development. Pre-clinical investigations are currently ongoing to try to identify the root cause for these observed differences. A comprehensive data pack will be available in 1H2013 to allow planning for the next steps.

CHMP's comment: The MAH's results are awaited for further evaluation.