PUBLIC ASSESSMENT SUMMARY REPORT - HEXAXIM®

What is HEXAXIM®?

HEXAXIM®, (DTaP-HepB-IPV-Hib), is a fully liquid hexavalent vaccine composed of diphtheria, tetanus, pertussis (acellular component), hepatitis B (rDNA), poliomyelitis (inactivated) and haemophilus influenza type b conjugate vaccine (adsorbed) produced by Sanofi Pateur, France
with the following composition:

Ingredient	Concentration per 0.5 mL dose	Function
Diphtheria toxoid	30 Lf (≥ 20 IU†)	Active Ingredient
Tetanus toxoid	10 Lf (≥ 40 IU†)	Active Ingredient
Bordetella pertussis antigens Pertussis toxoid Filamentous haemagglutinin	 25 µg 25 µg	Active Ingredient
Polio virus (Mahoney) Type 1 ‡ Polio virus (MEF-1) Type 2 ‡ Polio virus (Saukett) Type 3 ‡	40 D-antigen units 8 D-antigen units 32 D-antigen units	Active Ingredient
Hepatitis B surface antigen**	10 µg	Active Ingredient
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate) conjugated to Tetanus protein (PRP-T)	12 µg 22-36 µg	Active Ingredient
Aluminium hydroxide, hydrated, for adsorption	0.6 mg Al3+	Adjuvant
Buffer solution Water for injection	 Up to 0.5 mL	Neutralization and osmolality and adjustment

† As lower confidence limit (p = 0.95)
‡ Produced on Vero cells
** Produced in yeast *Hansenula polymorpha* cells by recombinant DNA technology

The presentations to be made available to UN agencies are boxes of 10 unidoses glass vials (0.5 ml).

A VVM7 is attached to the label. The vaccine has a shelf-life of 36 months at 2-8°C.
Due to the lack of more appropriate VVM for this product and during the development of a better device, as a temporary measure, VVM type 7 is accepted, in principle, for use with this product. However VVM7 reaches its expiry after 2 years 8 months at 5°C and 1 year 8 months at 8°C. Therefore, there is a concern

that the VVM on batches of vaccine supplied could reach its expiry point while the vaccine is still within its expiry date, leading to vaccine wastage.

What is HEXAXIM® used for?

Hexaxim® is indicated for primary and booster vaccination of infants from six weeks of age against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and invasive infections caused by Haemophilus influenzae type b (such as meningitis, septicaemia, cellulitis, arthritis, epiglottitis, pneumopathy, osteomyelitis).

How is HEXAXIM® used?

Hexaxim is a whitish, cloudy suspension that should be administered intramuscularly. The recommended injection sites are generally the antero-lateral aspect of the upper thigh in infants and toddlers and the deltoid muscle in older children.

Primary vaccination:
The primary vaccination schedule consists of three doses of 0.5 ml (such as 6, 10, 14 weeks; 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) to be administered at intervals of at least four weeks, in accordance with official recommendations.
All vaccination schedules including the Expanded Program on Immunisation (at 6, 10, 14 weeks of age) can be used whether or not a dose of hepatitis B vaccine has been given at birth.
Where a dose of hepatitis B vaccine is given at birth, Hexaxim can be used for supplementary doses of hepatitis B vaccine from the age of six weeks. If a second dose of hepatitis B vaccine is required before this age, monovalent hepatitis B vaccine should be used.

Booster vaccination:
After primary vaccination (e.g. 6, 10, 14 weeks; 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) with Hexaxim, a booster dose of HepB and Hib must be administered during the second year of life and at least 6 months after the last priming dose.
In addition, if the priming schedule used is 6, 10 and 14 weeks a booster dose of polio vaccine should be given. Hexaxim or any other vaccine containing HepB, Hib and, if necessary, polio antigens may be used to accomplish boosting of the immune responses to these antigens.

Booster doses should be given in accordance with the official recommendations.

Paediatric population

The safety and efficacy of Hexaxim in children over 24 months of age have not been established.

What are the vaccine characteristics?

HEXAXIM® must be stored at 2-8°C. Under these recommended storage conditions, the vaccine is stable for 36 months after the date of manufacture. It should not be frozen.

Who is the regulatory authority responsible for its oversight vis a vis WHO?

The NRA of record is the European Medicines Agency (www.ema.europa.eu/ema)

How has HEXAXIM® been studied from the clinical point of view?

The priming schedules have been used in the following countries: 6-10-14 weeks with and without hepatitis B at birth (Republic of South Africa); 2-3-4 months without hepatitis B at birth (Turkey);

2,4,6 months without hepatitis B at birth (Argentina, Mexico, Peru); 2,4,6 months with hepatitis B at birth (Costa Rica and Colombia).
Results obtained in these clinical studies for each of the components showed that the percentage of subjects with antibody titres ≥ seroprotection/seroconversion rates* one
month after a 3 doses primary vaccination with Hexaxim was satisfactory. Same observation was made with the percentage of subjects with antibody titres ≥ seroprotection/seroconversion rates* one month after booster vaccination with Hexaxim

Vaccine efficacy of the acellular pertussis (aP) antigens contained in Hexaxim against the most severe WHO-defined typical pertussis (≥ 21 days of paroxysmal cough) is documented in a randomized double-blind study among infants with a 3 dose primary series using a DTaP vaccine in a highly endemic country (Senegal). The need for a toddler booster dose was seen in this study.
The long term capability of the acellular pertussis (aP) antigens contained in Hexaxim to reduce pertussis incidence and control pertussis disease has been demonstrated in a 10-year national pertussis surveillance on pertussis disease in Sweden with the Pentavac/Pentaxim vaccine.
The vaccine effectiveness against Hib invasive disease of DTaP and Hib combination vaccines (pentavalent and hexavalent including vaccines containing the Hib antigen from Hexaxim) has been demonstrated in Germany via an extensive (over five years follow-up period) post-marketing surveillance study. The vaccine effectiveness was of 96.7% for the full primary series, and 98.5% for booster dose (irrespective of priming).

Data on concomitant administration of Hexaxim with a pneumococcal polysaccharide conjugated vaccine have shown no clinically relevant interference in the antibody response to each of the antigens.
Data on concomitant administration of a booster dose of Hexaxim with measles-mumps-rubella vaccines have shown no clinically relevant interference in the antibody response to each of the antigens. There may be a clinically relevant interference in the antibody response of Hexaxim and Varilrix and these vaccines should not be administered at the same time.
Data on concomitant administration of Hexaxim with rotavirus vaccines have shown no clinically relevant interference in the antibody response to each of the antigens.
Hexaxim must not be mixed with other vaccines or other parenterally administered drugs.
Separate injection sites must be used in case of concomitant administration.

Except in the case of immunosuppressive therapy, no significant clinical interaction with other treatments or biological products has been reported.

Other information about evaluation of HEXAXIM® :

Hexaxim was granted a scientific opinion by EMA under Article 58 procedure.
The process for evaluation of Hexaxim® for prequalification by WHO followed the streamlined procedure described in the document "Procedure for assessing the acceptability, in principle, of vaccines for purchase by United Nations Agencies" (**WHO TRS 978, Annex 6**).
The approval of the DTaP-Hep B-IPV-Hib vaccine was based on the review of EMA reports related to the quality, safety and efficacy data including evaluation of the consistency of the vaccine, the satisfactory outcome of a joint EMA/WHO site audit of the vaccine manufacturing facilities in Argentina, the review and approval of ongoing variations and the full implementation of the recommendations made by WHO during the evaluation process related to the compliance with the UN tender specifications.

This summary was last updated on 10 February 2015