1. NAME OF THE MEDICINAL PRODUCT

Hexaxim suspension for injection in pre-filled syringe

Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated) and *Haemophilus influenzae* type b conjugate vaccine (adsorbed).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose[1] (0.5 ml) contains:

Diphtheria Toxoid	not less than 20 IU[2]
Tetanus Toxoid	not less than 40 IU[2,3]
Bordetella pertussis antigens	
Pertussis Toxoid	25 micrograms
Filamentous Haemagglutinin	25 micrograms
Poliovirus (Inactivated)[4]	
Type 1 (Mahoney)	40 D antigen units[5]
Type 2 (MEF-1)	8 D antigen units[5]
Type 3 (Saukett)	32 D antigen units[5]
Hepatitis B surface antigen[6]	10 micrograms
Haemophilus influenzae type b polysaccharide (Polyribosylribitol Phosphate) conjugated to Tetanus protein	12 micrograms 22-36 micrograms

[1] Adsorbed on aluminium hydroxide, hydrated (0.6 mg Al^{3+})
[2] As lower confidence limit (p= 0.95)
[3] Or equivalent activity determined by an immunogenicity evaluation
[4] Produced on Vero cells
[5] Or equivalent antigenic quantity determined by a suitable immunochemical method
[6] Produced in yeast *Hansenula polymorpha* cells by recombinant DNA technology

The vaccine may contain traces of glutaraldehyde, formaldehyde, neomycin, streptomycin and polymyxin B which are used during the manufacturing process (see section 4.3).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe.

Hexaxim is a whitish, cloudy suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Hexaxim (DTaP-IPV-HB-Hib) is indicated for primary and booster vaccination of infants and toddlers from six weeks to 24 months of age against diphtheria, tetanus, pertussis,

hepatitis B, poliomyelitis and invasive diseases caused by *Haemophilus influenzae* type (Hib).

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Primary vaccination:

The primary vaccination consists of three doses of 0.5 ml to be administered at intervals of at least four weeks and as per schedules 6, 10, 14 weeks; 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months.

All vaccination schedules including the WHO Expanded Program on Immunisation (EPI) 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.

When a dose of hepatitis B vaccine is given at birth, the sequential infant primary vaccination hexavalent/ pentavalent/ hexavalent schedule with Hexaxim and a pentavalent DTaP-IPV/Hib vaccine can be used in accordance with official recommendations.

The use of this vaccine should be in accordance with official recommendations.

Booster vaccination:

After a 3-dose primary vaccination with Hexaxim, a booster dose should be given, preferably during the second year of life, at least 6 months after the last priming dose.

Booster doses should be given in accordance with the official recommendations. At the very least, a dose of Hib vaccine must be administered.

After a 3-dose primary vaccination with Hexaxim (2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) and in the absence of hepatitis B vaccination at birth, it is necessary to give a hepatitis B vaccine booster dose. Hexaxim can be considered for the booster.

After a 3-dose WHO EPI schedule with Hexaxim (6, 10, 14 weeks) and in the absence of hepatitis B vaccination at birth, a hepatitis B vaccine booster must be given. At the very least, a booster dose of polio vaccine should be given. Hexaxim can be considered for the booster.

When a hepatitis B vaccine is given at birth, after a 3-dose primary vaccination, Hexaxim or a pentavalent DTaP-IPV/Hib vaccine can be administered for the booster.

Hexaxim may be used as a booster in individuals who have previously been vaccinated with another hexavalent vaccine or a pentavalent DTaP-IPV/Hib vaccine associated with a monovalent hepatitis B vaccine.

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

Methodofadministration

Immunisation must be carried out by intramuscular (IM) injection. The recommended injection site is preferably the antero-lateral area of the upper thigh and the deltoid muscle in older children (possibly from 15 months of age).

For instructions on handling see section 6.6.

4.3 Contraindications

History of an anaphylactic reaction after a previous administration of Hexaxim.

Hypersensitivity to the active substances, to any of the excipients listed in section 6.1, to trace residuals (glutaraldehyde, formaldehyde, neomycin, streptomycin and polymyxin B), to any pertussis vaccine, or after previous administration of Hexaxim or a vaccine containing the same components or constituents.

Vaccination with Hexaxim is contraindicated if the individual has experienced an encephalopathy of unknown aetiology, occurring within 7 days following prior vaccination with a pertussis containing vaccine (whole cell or acellular pertussis vaccines).
In these circumstances pertussis vaccination should be discontinued and the vaccination course should be continued with diphtheria, tetanus, hepatitis B, poliomyelitis and Hib vaccines.

Pertussis vaccine should not be administered to individuals with progressive neurologic disorder, uncontrolled epilepsy or progressive encephalopathy until treatment for the condition has been established, the condition has stabilised and the benefit clearly outweighs the risk.

4.4 Special warnings and precautions for use

Hexaxim will not prevent disease caused by pathogens other than *Corynebacterium diphtheriae*, *Clostridium tetani*, *Bordetella pertussis*, hepatitis B virus, poliovirus or *Haemophilus influenzae* type b. However, it can be expected that hepatitis D will be prevented by immunisation as hepatitis D (caused by the delta agent) does not occur in the absence of hepatitis B infection.

Hexaxim will not protect against hepatitis infection caused by other agents such as hepatitis A, hepatitis C and hepatitis E or by other liver pathogens.

Because of the long incubation period of hepatitis B, it is possible for unrecognised hepatitis B infection to be present at the time of vaccination. The vaccine may not prevent hepatitis B infection in such cases.

Hexaxim does not protect against infectious diseases caused by other types of *Haemophilus influenzae* or against meningitis of other origins.

Priortoimmunisation

Immunisation should be postponed in individuals suffering from moderate to severe acute febrile illness or infection. The presence of a minor infection and/or low-grade fever should not result in the deferral of vaccination.

Vaccination should be preceded by a review of the person's medical history (in particular previous vaccinations and possible adverse reactions). The administration of Hexaxim must be

carefully considered in individuals who have a history of serious or severe reactions within 48 hours following administration of a vaccine containing similar components.

Before the injection of any biological, the person responsible for administration must take all precautions known for the prevention of allergic or any other reactions. As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following administration of the vaccine.

If any of the following events are known to have occurred after receiving any pertussis containing vaccine, the decision to give further doses of pertussis containing vaccine should be carefully considered:

- Temperature of $\geq 40°C$ within 48 hours not due to another identifiable cause;
- Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours of vaccination;
- Persistent, inconsolable crying lasting ≥ 3 hours, occurring within 48 hours of vaccination;
- Convulsions with or without fever, occurring within 3 days of vaccination.

There may be some circumstances, such as high incidence of pertussis, when the potential benefits outweigh possible risks.

A history of febrile convulsions, a family history of convulsions or Sudden Infant Death Syndrome (SIDS) do not constitute a contraindication for the use of Hexaxim. Individuals with a history of febrile convulsions should be closely followed up as such adverse events may occur within 2 to 3 days post vaccination.

If Guillain-Barré syndrome or brachial neuritis has occurred following receipt of prior vaccine containing tetanus toxoid, the decision to give any vaccine containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks, such as whether or not the primary vaccination has been completed. Vaccination is usually justified for individuals whose primary vaccination is incomplete (i.e. fewer than three doses have been received).

Some case reports of multiple sclerosis have been reported after administration of hepatitis B vaccine. To date a causal relationship has not been demonstrated with hepatitis B vaccine.

The immunogenicity of the vaccine may be reduced by immunosuppressive treatment or immunodeficiency. It is recommended to postpone vaccination until the end of such treatment or disease. Nevertheless, vaccination of individuals with chronic immunodeficiency such as HIV infection is recommended even if the antibody response may be limited.

Specialpopulations

No data are available for premature infants. However, a lower immune response may be observed and the level of clinical protection is unknown.

Immune responses to the vaccine have not been studied in the context of genetic polymorphism.

In individuals with chronic renal failure, an impaired hepatitis B response is observed and administration of additional doses of hepatitis B vaccine should be considered according to the antibody level against hepatitis B virus surface antigen (anti-HBsAg).

Precautionsforuse

Do not administer by intravascular, intradermal or subcutaneous injection.

As with all injectable vaccines, the vaccine must be administered with caution to individuals with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration.

The potential risk of apnoea and the need for respiratory monitoring for 48 to 72 hours should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

In an open-label, randomized controlled trial done in South Africa where either Hexaxim or a control vaccine (Combact-Hib+OPV) was concomitantly administered with MMR and varicella vaccine to children 15-18 months of age, the varicella response [≥300 mIU/mL (ELISA) or ≥4 1/dil (FAMA)] for both Hexaxim and control groups (73.8% and 72.5% respectively) was lower than would be expected after a single dose of varicella vaccines in healthy children. No comparison of concomitant use versus administration at different time points has been performed. Thus, although this may reflect age-dependent immune responses to varicella vaccines, there may be clinically relevant interference in the antibody response of Hexaxim and a varicella vaccine and these vaccines should not be administered at the same time.

When Hexaxim was co-administered with Prevenar 13 (pneumococcal polysaccharide conjugated vaccine, adsorbed) in one clinical trial, data indicated that the percentage of subjects experiencing solicited reactions and unsolicited AEs was similar to the control group which was given Prevenar 13 and another acellular pertussis-based hexavalent vaccine (Infanrix Hexa). A similar proportion of subjects experienced solicited systemic reactions with the exception of pyrexia (rectal temperature ≥ 38.0°C), which had a higher incidence for the Hexaxim group (82.3%) than the control group (69.0%). Especially post dose 1, pyrexia was higher in Hexaxim group (46.3%) than the control group (26.3%), which comprises mainly Grade 1 and Grade 2 pyrexia (rectal temperature 38.0 to 39.5 ^{o}C). Appropriate counselling for the parents is therefore recommended. (see 4.8 Undesirable effects).

Interferencewithlaboratorytesting

Since the Hib capsular polysaccharide antigen is excreted in the urine, a positive urine test can be observed within 1 to 2 weeks following vaccination. Other tests should be performed in order to confirm Hib infection during this period.

4.5 Interaction with other medicinal products and other forms of interaction

Data on concomitant administration of Hexaxim with a pneumococcal polysaccharide conjugate vaccine have shown no clinically relevant interference in the antibody response to each of the antigens. High incidence of fever (any grade) was reported in a study on concomitant administration with Prevenar 13. (see section 4.4)

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 a varicella vaccine and these vaccines should not be administered at the same time. (see section 4.4)

Data on concomitant administration of rotavirus vaccines 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 a meningococcal group A, C, W-135 and Y conjugate vaccine have shown no clinically relevant interference in the antibody response to each of the antigens.

If co-administration with another vaccine is considered, immunization should be carried out on separate injections sites.

Hexaxim must not be mixed with any other vaccines or other parenterally administered medicinal products.

No significant clinical interaction with other treatments or biological products has been reported except in the case of immunosuppressive therapy (see section 4.4).

Interferencewithlaboratorytesting: see section 4.4.

4.6 Fertility, pregnancy and lactation

Not applicable. This vaccine is not intended for administration to women of child-bearing age.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

a-Summaryofthesafetyprofile
Data from 5,823 subjects exposed to Hexaxim from completed clinical trials have been used to summarize the safety profile. In clinical studies in individuals who received Hexaxim, the most frequently reported reactions include injection-site pain, irritability, crying, and injection-site erythema.
Slightly higher solicited reactogenicity was observed after the first dose compared to subsequent doses.

b-Tabulatedlistofadversereactions
The following convention has been used for the classification of adverse reactions;
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from available data)

Table 1: Adverse Reactions from clinical trials and reported during commercial use

System Organ Class	Frequency	Adverse Events
Immune system disorders	Uncommon	Hypersensitivity reaction
	Rare	Anaphylactic reaction*
Metabolism and nutrition disorders	Very common	Anorexia (decreased appetite)

Nervous system disorders	Very common	Crying, somnolence
	Common	Abnormal crying (prolonged crying)
	Rare	Convulsions with or without fever*
	Very rare	Hypotonic reactions or hypotonic-hyporesponsive episodes (HHE)
Gastrointestinal disorders	Very common	Vomiting
	Common	Diarrhoea
Skin and subcutaneous tissue disorders	Rare	Rash
General disorders and administration site conditions	Very common	Injection-site pain, injection-site erythema, injection-site swelling Irritability Pyrexia (body temperature ≥ 38.0°C)
	Common	Injection-site induration
	Uncommon	Injection-site nodule Pyrexia (body temperature ≥39.6°C)
	Rare	Extensive limb swelling†

* Adverse reactions from spontaneous reporting.
† See section c.

c-Descriptionofselectedadversereactions
Extensive limb swelling: Large injection-site reactions (>50 mm), including extensive limb swelling from the injection site beyond one or both joints, have been reported in children. These reactions start within 24-72 hours after vaccination, may be associated with erythema, warmth, tenderness or pain at the injection site and resolve spontaneously within 3-5 days. The risk appears to be dependent on the number of prior doses of acellular pertussis containing vaccine, with a greater risk following the 4th and 5th doses.

Pyrexia: When Hexaxim was co-administered with Prevenar 13 (pneumococcal polysaccharide conjugated vaccine, adsorbed) in one clinical trial, data indicated that the percentage of subjects experiencing solicited reactions and unsolicited AEs was similar to the control group given Prevenar 13 and another acellular pertussis-based hexavalent vaccine (Infanrix Hexa). A similar proportion of subjects experienced solicited systemic reactions with the exception of pyrexia (rectal temperature ≥38.0°C), which had a higher incidence for the Hexaxim group (82.3%) than the control group (69.0%). Especially post dose 1, pyrexia was higher in Hexaxim group (46.3%) than the control group (26.3%), which comprises mainly Grade 1 and 2 pyrexia (rectal temperature 38.0 to 39.5 ^{o}C)

d- Potential adverse events (i.e. adverse events which have been reported with other vaccines containing one or more of the components or constituents of Hexaxim and not directly with Hexaxim)

Nervous system disorders
- Brachial neuritis and Guillain-Barré Syndrome have been reported after administration of a tetanus toxoid containing vaccine
- Peripheral neuropathy (polyradiculoneuritis, facial paralysis), optic neuritis, central nervous system demyelination (multiple sclerosis) have been reported after administration of a hepatitis B antigen containing vaccine
- Encephalopathy/encephalitis

Respiratory, thoracic and mediastinal disorders
Apnoea in very premature infants (≤ 28 weeks of gestation) (see section 4.4)

General disorders and administration site conditions
Oedematous reaction affecting one or both lower limbs may occur following vaccination with *Haemophilus influenzae* type b containing vaccines. If this reaction occurs, it is mainly after primary injections and within the first few hours following vaccination. Associated symptoms may include cyanosis, redness, transient purpura and severe crying. All events should resolve spontaneously without sequel within 24 hours.

Reportingofsuspectedadversereactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

4.9 Overdose

No cases of overdose have been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Vaccines, Bacterial and viral vaccines combined, ATC code: J07CA09

The primary vaccination schedules that have been used are: 6, 10, 14 weeks with and without hepatitis B vaccination at birth; 2, 3, 4 months without hepatitis B vaccination at birth; 2, 4, 6 months with and without hepatitis B vaccination at birth.

Results obtained for each of the components are summarised in the tables below:

Table 2: Seroprotection/Seroconversion rates* one month after primary vaccination with 3 doses of Hexaxim

Antibody Thresholds	**6-10-14 Weeks**	**2-3-4 Months**	**2-4-6 Months**
	N=123 to 220†	**N=322††**	**N=934 to 1270‡**
	%	**%**	**%**
Anti-diphtheria (> 0.01 IU/ml)	97.6	99.7	97.1
Anti-tetanus (≥ 0.01 IU/ml)	100.0	100.0	100.0
Anti-PT (Seroconversion ‡‡) (Vaccine response§)	 93.6 100.0	 88.3 99.4	 96.0 99.7
Anti-FHA (Seroconversion ‡‡) (Vaccine response§)	 93.1 100.0	 90.6 99.7	 97.0 99.9

Anti-HBs (≥ 10 mIU/ml)	With hepatitis B vaccination at birth	99.0	/	99.7
	Without hepatitis B vaccination at birth	95.7	96.8	98.8
Anti-Polio type 1 (≥ 8 (1/dilution))		100.0	99.4	99.9
Anti-Polio type 2 (≥ 8 (1/dilution))		98.5	100.0	100.0
Anti-Polio type 3 (≥ 8 (1/dilution))		100.0	99.7	99.9
Anti-PRP (≥ 0.15 µg/ml)		95.4	96.2	98.0

* Generally accepted surrogates (PT, FHA) or correlates of protection (other components)
N = Number of individuals analysed (per protocol set)
† 6, 10, 14 weeks with and without hepatitis B vaccination at birth (Republic of South Africa) Study A3L15
†† 2, 3, 4 months without hepatitis B vaccination at birth (Finland) Study A3L43-EXT (HXM01C-PS)
‡ 2, 4, 6 months without hepatitis B vaccination at birth (Argentina, Mexico, Peru) and with hepatitis B vaccination at birth (Costa Rica and Colombia) –Studies A3L02, A3L11, A3L24
‡‡ Seroconversion: minimum 4-fold increase compared to pre-vaccination level (pre-dose 1)
§ Vaccine response: If pre-vaccination antibody concentration <8 EU/ml, then the post-vaccination antibody concentration should be ≥8 EU/ml. Otherwise, post-vaccination antibody concentration should be ≥ pre-immunisation level

Table 3: Seroprotection/Seroconversion rates *one month after booster vaccination with Hexaxim

Antibody Thresholds		**Booster vaccination during the second year of life following a three dose primary course**		
		6-10-14 Weeks	**2-3-4 Months**	**2-4-6 Months**
		N=204†	N=178††	N=177 to 396‡
		%	**%**	**%**
Anti-diphtheria (≥ 0.1 IU/ml)		100.0	100.0	97.2
Anti-tetanus (≥ 0.1 IU/ml)		100.0	100.0	100.0
Anti-PT (Seroconversion‡‡) (Vaccine response§)		94.4 100.0	86.0 98.8	96.2 100.0
Anti-FHA (Seroconversion‡‡) (Vaccine response§)		99.4 100.0	94.3 100.0	98.4 100.0
Anti-HBs (≥ 10 mIU/ml)	With hepatitis B vaccination at birth	100.0	/	99.7
	Without hepatitis B vaccination at birth	98.5	98.9	99.4
Anti-Polio type 1 (≥ 8 (1/dilution))		100.0	98.9	100.0
Anti-Polio type 2 (≥ 8 (1/dilution))		100.0	100.0	100.0
Anti-Polio type 3 (≥ 8 (1/dilution))		100.0	100.0	100.0
Anti-PRP (≥ 1.0 µg/ml)		98.5	98.9	98.3

* Generally accepted surrogates (PT, FHA) or correlates of protection (other components)
N = Number of individuals analysed (per protocol set)
† 6, 10, 14 weeks with and without hepatitis B vaccination at birth (Republic of South Africa) Study A3L15
†† 2, 3, 4 months without hepatitis B vaccination at birth (Finland) Study A3L43-EXT (HXM01C-Booster)
‡ 2, 4, 6 months without hepatitis B vaccination at birth (Mexico) and with hepatitis B vaccination at birth (Costa Rica and Colombia) – Studies A3L21, A3L27
‡‡ Seroconversion: minimum 4-fold increase compared to pre-vaccination level (pre-dose 1)
§ Vaccine response: If pre-vaccination antibody concentration (pre-dose 1) <8 EU/ml, then the post-booster antibody concentration should be ≥8 EU/ml. Otherwise, post-booster antibody concentration should be ≥ pre-immunisation level (pre-dose 1)

Persistenceofimmuneresponse

Studies on long-term persistence of vaccine induced antibodies following varying infant / toddler primary series and following Hepatitis B vaccine given at birth or not have shown maintenance of levels above the recognized protective levels or antibody thresholds for the vaccine antigens (see Table 4). In addition, immunity against the hepatitis B component of the vaccine has been shown to persist up to 9 years of age after a primary series consisting of one dose of Hepatitis B vaccine given at birth followed by a 3-dose infant series at 2, 4, and 6 months of age without a toddler booster where 49.3% of vaccinees had antibodies ≥ 10 mIU/ml with geometric mean concentrations at 13.3 (95% CI: 8.82 – 20.0) mIU/ml. Immune memory against Hepatitis B had been demonstrated by the presence of an anamnestic response to a challenge Hepatitis B vaccination at the age of 9 years in 93% of vaccinees with development of geometric mean concentrations at 3692 (95% CI: 1886 – 7225) mIU/ml after vaccination.

Table 4: Seroprotection rates[a] at the age of 4.5 years old after vaccination with Hexaxim

Antibody Thresholds	Primary 6-10-14 weeks and booster at 15-18 months		Primary 2-4-6 months and booster at 12-24 months
	Without hepatitis B at birth	With hepatitis B at birth	With hepatitis B at birth
	N = 173[b]	N = 103[b]	N = 220[c]
	%	%	%
Anti-diphtheria (≥ 0.01 IU/ml) (≥ 0.1 IU/ml)	98.2 75.3	97 64.4	100 57.2
Anti-tetanus (≥ 0.01 IU/ml) (≥ 0.1 IU/ml)	100 89.5	100 82.8	100 80.8
Anti-PT[e] (≥ 8 EU/ml)	42.5	23.7	22.2
Anti-FHA[e] (≥ 8 EU/ml)	93.8	89.0	85.6
Anti-HBs (≥ 10 mIU/ml)	73.3	96.1	92.3
Anti-Polio type 1 (≥ 8 (1/dilution))	NA[d]	NA[d]	99.5
Anti-Polio type 2 (≥ 8 (1/dilution))	NA[d]	NA[d]	100
Anti-Polio type 3 (≥ 8 (1/dilution))	NA[d]	NA[d]	100
Anti-PRP (≥ 0.15 μg/ml)	98.8	100	100

N= Number of individuals analysed (per protocol set)
a: Generally accepted surrogates (PT, FHA) or correlates of protection (other components)
b: 6, 10, 14 weeks with and without hepatitis B vaccination at birth (Republic of South Africa)
c: 2, 4, 6 months with hepatitis B vaccination at birth (Colombia)
d: Due to an OPV National Immunisation Days in the country, Polio results have not have been analysed
e: 8 EU/ml corresponds to 4 LLOQ (Lower Limit Of Quantification in enzyme-linked immunosorbent assay ELISA).
LLOQ value for anti-PT and anti-FHA is 2 EU/ml

Efficacyandeffectivenessinprotectingagainstpertussis

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 randomised 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 in the childhood has been demonstrated in a 10-year national pertussis surveillance on pertussis disease in Sweden with the pentavalent DTaP-IPV/Hib vaccine using a 3, 5, 12 months schedule. Results of long term follow-up demonstrated a dramatic reduction of the pertussis incidence following the second dose regardless of the vaccine used.

EffectivenessinprotectingagainstHibinvasivedisease

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).

5.2 Pharmacokinetic properties

No pharmacokinetic studies have been performed.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional repeat dose toxicity and local tolerance studies.

At the injection sites, chronic histological inflammatory changes were observed, that are expected to have a slow recovery.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium hydrogen phosphate
Potassium dihydrogen phosphate
Trometamol
Saccharose
Essential amino acids including L-phenylalanine
Sodium hydroxide, acetic acid or hydrochloric acid (for pH adjustment)
Water for injections.

For adsorbent: see section 2.

6.2 Incompatibilities

In the absence of compatibility studies, this vaccine must not be mixed with other vaccines or medicinal products.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).
Do not freeze.
Keep the container in the outer carton in order to protect from light.

Stability data indicate that the vaccine components are stable at temperatures up to 25°C for 72 hours. At the end of this period, Hexaxim should be used or discarded. These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

6.5 Nature and contents of container

0.5 ml suspension in pre-filled syringe (type I glass) with plunger stopper (halobutyl) and tip cap (halobutyl), without needle.
0.5 ml suspension in pre-filled syringe (type I glass) with plunger stopper (halobutyl) and tip cap (halobutyl), with 1 separate needle.
0.5 ml suspension in pre-filled syringe (type I glass) with plunger stopper (halobutyl) and tip cap (halobutyl), with 2 separate needles.

Pack size of 1 or 10.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Prior to administration, the pre-filled syringe should be shaken in order to obtain a homogeneous, whitish, cloudy suspension.

The suspension should be visually inspected prior to administration. In the event of any foreign particulate matter and/or variation of physical aspect being observed, discard the pre-filled syringe.

For syringes without an attached needle, the needle must be fitted firmly to the syringe, rotating it by a one-quarter turn.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Sanofi Pasteur
14 Espace Henry Vallée
69007 Lyon
France

8. DATE OF REVISION OF THE TEXT

24 July 2019 (Based on the EU SmPC 03/2019)