HEXAXIM

Suspension for injection

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

COMPOSITION

One dose[1] (0.5 ml) contains:

Diphtheria Toxoid	not less than 20 IU[2,4] (30 Lf)
Tetanus Toxoid	not less than 40 IU[3,4] (10 Lf)
Bordetella pertussis antigens	
Pertussis Toxoid	25 micrograms
Filamentous Haemagglutinin	25 micrograms
Poliovirus (Inactivated)[5]	
Type 1 (Mahoney)	29 D antigen units[6]
Type 2 (MEF-1)	7 D antigen units[6]
Type 3 (Saukett)	26 D antigen units[6]
Hepatitis B surface antigen[7]	10 micrograms
Haemophilus influenzae type b polysaccharide (Polyribosylribitol Phosphate) conjugated to Tetanusprotein	12 micrograms 22 -36 micrograms

[1] Adsorbed on aluminium hydroxide, hydrated (0.6 mg Al^{3+})
[2] As lower confidence limit (p= 0.95) and not less than 30 IU as mean value
[3] As lower confidence limit (p= 0.95)
[4] Or equivalent activity determined by an immunogenicity evaluation
[5] Cultivated on Vero cells
[6] These antigen quantities are strictly the same as those previously expressed as 40-8-32 D-antigen units, for virus type 1, 2 and 3 respectively, when measured by another suitable immunochemical method
[7] 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 Contraindications).

Excipient with known effect
Phenylalanine……85 micrograms
(See section Special warnings and precautions for use)

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

THERAPEUTIC INDICATION

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 b (Hib).

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

POSOLOGY AND METHOD OF ADMINISTRATION

Posology

Primary vaccination:

The primary vaccination consists of 3 doses of 0.5 mL to be administered at intervals of at least four weeks and as per schedules 6, 10, 14 weeks; 2, 4, 6 months and 2, 3, 4 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.
- The use of this vaccine should be in accordance with official recommendations.

Booster vaccination:

After a 3-dose primary vaccination with Hexaxim (6,10,14 weeks; 2,4,6 months and 2,3,4 months), 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.

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

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.

WHO-EPI schedule (6, 10, 14 weeks):

After a WHO-EPI schedule, a booster dose should be given

- As a minimum, a booster dose of polio vaccine should be given
- In absence of hepatitis B vaccine at birth, a hepatitis B vaccine booster must be given
- Hexaxim can be considered for the booster

Other paediatric population:

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

Method of administration

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

For instructions on handling, see section SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING.

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 uncontrolled neurologic disorder or uncontrolled epilepsy until treatment for the condition has been established, the condition has stabilised and the benefit clearly outweighs the risk.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

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.

Prior to immunisation
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 medicinal product, 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 ≥ 40°C within 48 hours of vaccination 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).

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.

Special populations:

Immunogenicity data are available for 105 preterm infants. These data support the use of Hexaxim in preterm infants. As expected in preterm infants, lower immune response has been observed for some antigens, when indirectly compared to term infants, although seroprotective levels have been achieved (see section Pharmacodynamic properties). No safety data were collected in preterm infants (born ≤ 37 weeks of gestation) in clinical trials.

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.

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).

Immunogenicity data in HIV-exposed infants (infected and uninfected) showed that Hexaxim is immunogenic in the potentially immunodeficient population of HIV-exposed infants whatever their HIV status at birth (see section Pharmacodynamic properties). No specific safety concern was observed in this population.

Precautions for use

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.

Syncope can occur following, or even before, any vaccination as a psychogenic response to the needle injection. Procedures should be in place to prevent falling and injury and to manage syncope.

Interference with laboratory testing
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.

Hexaxim contains phenylalanine, potassium and sodium
Hexaxim contains 85 micrograms phenylalanine in each 0.5 ml dose.
Phenylalanine may be harmful for individuals with phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.
Hexaxim contains less than 1 mmol potassium (39 mg) and less than 1 mmol sodium (23 mg) per dose, that is to say essentially "potassium free" and "sodium-free".

INTERACTIONS WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTIONS

Hexaxim can be administered simultaneously with a pneumococcal polysaccharide conjugate vaccine, measles, mumps, rubella (MMR) containing vaccines, rotavirus vaccines, a meningococcal C conjugate vaccine or a meningococcal group A, C, W-135 and Y conjugate vaccine, as no clinically relevant interference in the antibody response to each of the antigens have been shown.
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.
If co-administration with another vaccine is considered, immunisation should be carried out on separate injection sites.
Hexaxim must not be mixed with any other vaccines or other parenterally administered medicinal products.
Except in the case of immunosuppressive therapy (see section SPECIAL WARNING AND PRECAUTIONS FOR USE), no significant clinical interaction with other treatments or biological products has been reported
Interference with laboratory testing: see section SPECIAL WARNING AND PRECAUTIONS FOR USE.

Fertility, pregnancy and lactation
Not applicable. This vaccine is not intended for administration to women of child-bearing age.

Effects on ability to drive and use machines
Not applicable.

UNDESIRABLE EFFECTS

a. Summary of 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. Tabulated list of adverse reactions

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 post marketing surveillance

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	Pyrexia (body temperature ≥38.0°C) Irritability Injection-site pain, injection-site erythema, injection-site swelling
	Common	Injection-site induration
	Uncommon	Pyrexia (body temperature ≥39.6°C) Injection-site nodule
	Rare	Extensive limb swelling†

* Adverse reactions from spontaneous reporting.
† See section c. Description of selected adverse reactions

c. Description of selected adverse reactions
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 dose.

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).

Immune system disorders
- Anaphylactic reaction

Nervous system disorders
- Convulsion with or without fever
- Brachial neuritis and Guillain-Barré Syndrome have been reported after administration of a tetanus toxoid containing vaccine
- Peripheral neuropathy (polyradiculoneuritis, facialparalysis), 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 SPECIAL WARNING AND PRECAUTIONS FOR USE)

General disorders and administration site conditions
Oedematous reaction affecting one or both lower limbs may occur following vaccination with Haemophilus influenza 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.

Reporting of suspected adverse reactions
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 reaction via farmakovigilans@kalventis.com
and Pusat Farmakovigilans/MESO Nasional Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif Badan Pengawas Obat dan Makanan. Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079
Website: https://e-meso.pom.go.id/.

OVERDOSE
No cases of overdose have been reported.

PHARMACOLOGICAL PROPERTIES

Mechanism of action

The vaccine works by causing the body to produce its own protection (antibodies) against the bacteria and viruses.

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

Antibody Thresholds		Three doses		
		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 ‡‡)		93.6	88.3	96.0
(Vaccine response§)		100.0	99.4	99.7
Anti-FHA				
(Seroconversion ‡‡)		93.1	90.6	97.0
(Vaccine response§)		100.0	99.7	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)
†† 2, 3, 4 months without hepatitis B vaccination at birth (Finland)
‡ 2, 4, 6 months without hepatitis B vaccination at birth (Argentina, Mexico, Peru) and with hepatitis B vaccination at birth (Costa Rica and Colombia)
‡‡ 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 2: 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)
†† 2, 3, 4 months without hepatitis B vaccination at birth (Finland)
‡ 2, 4, 6 months without hepatitis B vaccination at birth (Mexico) and with hepatitis B vaccination at birth (Costa Rica and Colombia)
‡‡ 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)

Persistence of immune response

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 3).

Table 3: 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 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

The persistence of the immune response against the hepatitis B component of Hexaxim was evaluated in infants primed with different schedules.

For 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, 49.3% of children were

seroprotected (anti-HBsAg ≥ 10 mIU/mL) at 9 years of age, and 92.8% presented an anamnestic response after a challenge dose with a standalone Hepatitis B vaccine.
These data support persisting immune memory induced in infants primed with Hexaxim.

Immune responses to Hexaxim in preterm infants

Immune responses to Hexaxim antigens in preterm (105) infants (born after a gestation period of 28 to 36 weeks), including 90 infants born to women vaccinated with Tdap vaccine during pregnancy and 15 to women not vaccinated during pregnancy, were evaluated following a 3-dose primary vaccination course at 2, 3 and 4 months of age and a booster dose at 13 months of age.
One month after primary vaccination, all subjects were seroprotected against diphtheria (≥ 0.01 IU/mL), tetanus (≥ 0.01 IU/mL) and poliovirus types 1, 2 and 3 (≥ 8 (1/dilution)); 89.8% of subjects were seroprotected against hepatitis B (≥ 10 IU/mL) and 79.4% were seroprotected against Hib invasive diseases (≥ 0.15 µg/mL).
One month after the booster dose, all subjects were seroprotected against diphtheria (≥ 0.1 IU/mL), tetanus (≥ 0.1 IU/mL) and poliovirus types 1, 2 and 3 (≥ 8 (1/dilution)); 94.6% of subjects were seroprotected against hepatitis B (≥ 10 IU/mL) and 90.6% were seroprotected against Hib invasive diseases (≥ 1 µg/mL).
Regarding pertussis, one month after primary vaccination 98.7% and 100% of subjects developed antibodies ≥ 8 EU/mL against PT and FHA antigens respectively. One month after the booster dose 98.8% of subjects developed antibodies ≥ 8 EU/mL against both PT and FHA antigens. Pertussis antibody concentrations were increased by 13-fold after primary vaccination and by 6- to 14-fold after the booster dose.

Immune responses to Hexaxim in infants born to women vaccinated with Tdap during pregnancy

Immune responses to Hexaxim antigens in term (119) and preterm (90) infants born to women vaccinated with Tdap vaccine during pregnancy (between 24 and 36 weeks of gestation) were evaluated following a 3-dose primary vaccination course at 2, 3 and 4 months of age and a booster dose at 13 (preterm infants) or 15 (term infants) months of age.
One month after primary vaccination, all subjects were seroprotected against diphtheria (≥ 0.01 IU/mL), tetanus (≥ 0.01 IU/mL) and poliovirus types 1 and 3 (≥ 8 (1/dilution)); 97.3% of subjects were seroprotected against poliovirus type 2 (≥ 8 (1/dilution)); 94.6% of subjects were seroprotected against hepatitis B (≥ 10 IU/mL) and 88.0% were seroprotected against Hib invasive diseases (≥ 0.15 µg/mL).
One month after the booster dose, all subjects were seroprotected against diphtheria (≥ 0.1 IU/mL), tetanus (≥ 0.1 IU/mL) and poliovirus types 1, 2 and 3 (≥ 8 (1/dilution)); 93.9% of subjects were seroprotected against hepatitis B (≥ 10 IU/mL) and 94.0% were seroprotected against Hib invasive diseases (≥ 1 µg/mL).
Regarding pertussis, one month after primary vaccination 99.4% and 100% of subjects developed antibodies ≥ 8 EU/mL against PT and FHA antigens respectively. One month after the booster dose 99.4% of subjects developed antibodies ≥ 8 EU/mL against both PT and FHA antigens. Pertussis antibody concentrations were increased by 5- to 9-fold after primary vaccination and by 8- to 19-fold after the booster dose.

Immune responses to Hexaxim in HIV-exposed infants

Immune responses to Hexaxim antigens in 51 HIV-exposed infants (9 infected and 42 uninfected), were evaluated following a 3-dose primary vaccination course at 6, 10, and 14 weeks of age and a booster dose at 15 to 18 months of age.

One month after primary vaccination, all infants were seroprotected against diphtheria (≥ 0.01 IU/mL), tetanus (≥ 0.01 IU/mL) poliovirus types 1, 2 and 3 (≥ 8 (1/dilution), hepatitis B (≥ 10 IU/mL), and more than 97.6% for Hib invasive diseases (≥ 0.15 µg/mL).

One month after the booster dose, all subjects were seroprotected against diphtheria (≥ 0.1 IU/mL), tetanus (≥ 0.1 IU/mL), poliovirus types 1, 2 and 3 (≥ 8 (1/dilution), hepatitis B (≥ 10 IU/mL) and more than 96.6% for Hib invasive diseases (≥ 1 µg/mL).
Regarding pertussis, one month after primary vaccination, 100% of subjects developed antibodies ≥ 8 EU/mL against both PT and FHA antigens. One month after the booster dose, 100% of subjects developed antibodies ≥ 8 EU/mL against both PT and FHA antigens. Seroconversion rates defined as minimum 4-fold increase compared to pre-vaccination level (pre-dose 1) were 100% in the HIV-exposed and infected group for anti-PT and anti-FHA, and 96.6% for anti-PT and 89.7% for anti-FHA in the HIV-exposed and uninfected group.

Efficacy and effectiveness in protecting against pertussis

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.

Effectiveness in protecting against Hib invasive disease

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).

PHARMACOKINETICS PROPERTIES

No pharmacokinetic studies have been performed.

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.

INCOMPATIBILITY

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

SHELF LIFE

4 (four) years.

SPECIAL PRECAUTION FOR USE

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.

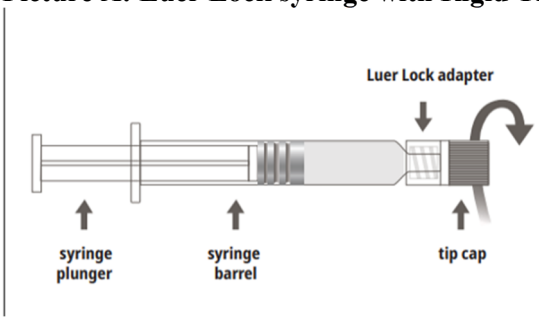
Special precautions for disposal and other handling
Prior to administration, the pre-filled syringe should be shaken in order to obtain a homogeneous, whitish, cloudy suspension.

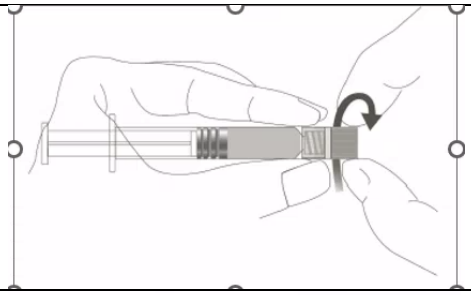
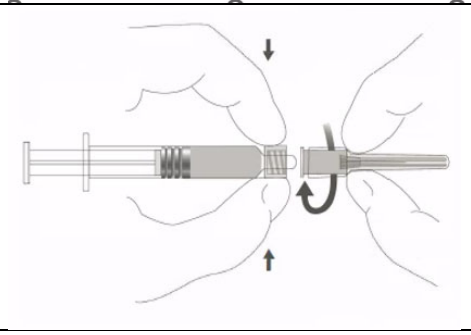
Preparation for administration
The syringe with suspension for injection should be visually inspected prior to administration. In the event of any foreign particulate matter, leakage, premature activation of the plunger or faulty tip seal, discard the pre-filled syringe.

The syringe is intended for single use only and must not be reused.

Instructions for use for the luer lock pre-filled syringe:

Picture A: Luer Lock syringe with Rigid Tip Cap



Step 1: Holding the Luer Lock adapter in one hand (avoid holding the syringe plunger or barrel), unscrew the tip cap by twisting it.	
Step 2: To attach the needle to the syringe, gently twist the needle into the Luer Lock adapter of the syringe until slight resistance is felt.	

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

PACKAGING PRESENTATION
0.5 mL -pack size of 1 pre-filled syringe @ 0.5 mL with 2 separate needles-
No. Reg.: DKI1459703243A1

Manufactured by: Sanofi Winthrop Industrie, Val-de-Reuil, France
Registered by: PT Kalventis Sinergi Farma,
Jakarta-Indonesia

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi

HARUS DENGAN RESEP DOKTER

sanofi

Based on BPOM approval dated XXX – Luer-Lock, CCDSv14, and Standar Informasi Obat

INFORMASI UNTUK PASIEN

HEXAXIM, Suspensi Injeksi dalam bentuk *prefilled syringe*

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

Bacalah isi seluruh selebaran ini dengan saksama sebelum anak Anda divaksinasi karena isi dalam selebaran ini mengandung informasi yang penting bagi mereka.

- Simpan leaflet ini. Anda mungkin perlu membacanya lagi.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker, atauperawat Anda.
- Jika anak Anda mengalami efek samping, konsultasikan dengan dokter, apoteker, atau perawat Anda. Efek tersebut mencangkup efek samping yang mungkin tidak tercantum dalam leaflet ini.

Apa isi yang terdapat dalam leaflet ini

1. Apakah HEXAXIM itu dan apakah kegunaannya

HEXAXIM (DTaP-IPV-HB-Hib) adalah sebuah vaksin yang digunakan untuk melindungi dari penyakit difteri, tetanus, pertussis, hepatitis B, poliomyelitis, dan penyakit-penyakit serius yang disebabkan oleh *Haemophilus influenzae* tipe b.

HEXAXIM diberikan kepada anak-anak usia antara enam minggu hingga 24 bulan.

Vaksin ini bekerja dengan menyebabkan tubuh membuat perlindungan sendiri (antibodi) terhadap bakteri dan virus yang menyebabkan berbagai infeksi berikut ini:

- Difteri adalah penyakit menular yang pertama kali biasanya mempengaruhi tenggorokan. Di tenggorokan, infeksi tersebut menyebabkan rasa sakit dan pembengkakan yang dapat menyebabkan kesulitan bernapas. Bakteri yang menyebabkan penyakit ini juga menghasilkan toksin (racun) yang menyebabkan kejang otot, yang menyebabkan ketidakmampuan untuk bernapas dan kemungkinan mati lemas.
- Tetanus (sering disebut kejang mulut / lockjaw) biasanya disebabkan oleh bakteri tetanus masuk secara dalam pada luka. Bakteri tersebut menghasilkan toksin (racun) yang menyebabkan kejang otot, yang menyebabkan ketidakmampuan untuk bernapas dan kemungkinan mati lemas.
- Pertussis (sering juga disebut batuk rejan) adalah penyakit yang sangat menular yang mempengaruhi saluran napas. Ini menyebabkan batuk parah yang dapat menimbulkan masalah pada pernapasan. Batuk ini sering menghasilkan suara seperti “Teriakan” suara. Batuk ini dapat berlangsung selama satu hingga dua bulan atau lebih. Batuk rejan juga bisa menyebabkan infeksi telinga, infeksi dada (bronkitis) yang mungkin bisa berlangsung lama, infeksi paru-paru (pneumonia), sawan (fits), kerusakan otak, dan bahkan kematian.
- Hepatitis B disebabkan oleh virus hepatitis B. Virus ini menyebabkan hati menjadi bengkak (meradang). Pada beberapa orang, virus ini dapat bertahan di dalam tubuh untuk waktu yang lama, dan akhirnya dapat menyebabkan masalah hati yang serius, termasuk kanker hati.
- Poliomielitis (sering hanya disebut polio) disebabkan oleh virus yang memengaruhi saraf. Virus ini dapat menyebabkan kelumpuhan atau kelemahan otot yang paling lazim adalah otot kaki. Kelumpuhan pada otot-otot yang mengendalikan otot untuk bernapas dan otot untuk menelan bisa berakibat fatal.
- Infeksi *Haemophilus influenzae* tipe b (sering hanya disebut Hib) adalah infeksi bakteri serius dan dapat menyebabkan meningitis (radang di penutup / selubung luar otak), yang dapat menyebabkan kerusakan otak, tuli, epilepsi, atau kebutaan parsial. Infeksi juga dapat menyebabkan peradangan dan pembengkakan di tenggorokan, sehingga menyebabkan kesulitan untuk menelan dan bernapas, dan infeksi dapat mempengaruhi bagian-bagian lain tubuh seperti darah, paru-paru, kulit, tulang dan sendi.

Informasi penting tentang perlindungan yang diberikan

- HEXAXIM hanya akan membantu mencegah penyakit-penyakit tersebut jika penyakit tersebut disebabkan oleh bakteri atau virus yang menjadi target vaksin ini. Anak Anda bisa terkena penyakit dengan gejala yang sama dengan yang disebabkan oleh bakteri atau virus lainnya.
- Vaksin ini tidak mengandung bakteri hidup atau virus dan tidak dapat menyebabkan suatu penyakit menular tertentu pada tubuh yang dilindunginya.
- Vaksin ini tidak melindungi dari infeksi yang disebabkan oleh *Haemophilus influenzae* jenis lain ataupun terhadap meningitis yang disebabkan oleh mikroorganisme.
- HEXAXIM tidak melindungi dari infeksi hepatitis yang disebabkan oleh agen-agen lain seperti hepatitis A, hepatitis C, dan hepatitis E.
- Karena gejala hepatitis B memerlukan waktu yang lama untuk berkembang, maka tetap dimungkinkan terjadinya infeksi hepatitis B pada saat vaksinasi. Vaksin ini tidak dapat mencegah infeksi hepatitis B jika terjadi kasus seperti itu.
- Seperti vaksin lainnya, Hexaxim mungkin tidak melindungi 100% anak yang menerima vaksin.

2. Apa yang perlu Anda ketahui sebelum HEXAXIM diberikan kepada anak Anda

Untuk memastikan bahwa HEXAXIM sesuai untuk anak Anda, merupakan hal yang penting untuk berkonsultasi dengan dokter atau perawat Anda jika terdapat poin-poin di bawah ini yang diberikan kepada anak Anda. Jika ada sesuatu yang Anda tidak mengerti, tanyakan kepada dokter, apoteker, atau perawat Anda untuk memberi penjelasan.

Jangan gunakan HEXAXIM jika anak Anda:

- Memiliki riwayat reaksi alergi (anafilaksis) yang antara lain ditandai dengan gangguan pernafasan dan pembengkakan wajah setelah pemberian HEXAXIM.
- Telah memiliki reaksi alergi :

- Terhadap zat aktif,
- Terhadap salah satu eksipien yang terdapat dalam bagian 6,
- Terhadap glutaraldehid, formaldehid, neomisin, streptomisin atau polimiksin B, karena zat-zat ini digunakan dalam pembuatan vaksin ini
- Setelah sebelumnya telah mendapatkan HEXAXIM atau vaksin difteri, tetanus, pertussis, poliomyelitis, hepatitis B atau vaksin yang mengandung Hib lainnya.

- Mengalami reaksi parah sehingga mempengaruhi otak (ensefalopati) dalam waktu 7 hari sebelum pemberian dosis vaksin pertussis (aselular atau pertussis sel keseluruhan).
- Memiliki gangguan saraf tidak terkontrol atau epilepsi tidak terkontrol.

Peringatan dan tindakan pencegahan

Berkonsultasilah dengan dokter, apoteker, atau perawat Anda sebelum melakukan vaksinasi jika anak Anda:

- Memiliki suhu badan sedang atau tinggi atau penyakit akut (seperti demam, sakit tenggorokan, batuk, pilek, atau flu). Vaksinasi HEXAXIM mungkin perlu ditunda hingga anak Anda telah lebih sehat.
- Telah mengalami salah satu dari kejadian berikut ini setelah mendapatkan vaksin pertussis, sehingga keputusan untuk memberikan dosis lanjutan berupa vaksin yang mengandung pertussis perlu dipertimbangkan:
    - Demam hingga 40ºC atau lebih dalam waktu 48 jam setelah vaksinasi bukan karena penyebab lain yang dapat diidentifikasi.
    - Pingsan atau kondisi yang menyerupai syok dengan episode hipotonik-hiporesponsif (penurunan energi) dalam waktu 48 jam setelah vaksinasi.
    - Menangis terus-menerus dan sulit dihentikan yang berlangsung selama 3 jam atau lebih, dan terjadi dalam waktu 48 jam setelah vaksinasi.
    - Kejang demam atau kejang tanpa demam yang terjadi dalam waktu 3 hari setelah vaksinasi.
    - Riwayat kejang demam, riwayat keluarga kejang atau kematian bayi mendadak (*Sudden Infant Death Syndrome/ SIDS*). Anak dengan riwayat kejang demam harus dimonitor 2-3 hari setelah vaksinasi.

- Sebelumnya mengalami sindrom Guillain-Barre (peradangan sementara pada saraf yang menyebabkan rasa sakit, kelumpuhan, dan gangguan sensitivitas) atau neuritis brakial (rasa sakit yang sangat parah dan penurunan mobilitas lengan dan bahu) setelah diberi vaksin yang mengandung toksoid tetanus (bentuk tidak aktif dari toksin tetanus). Dalam kasus ini, keputusan untuk memberikan vaksin yang mengandung toksoid tetanus lebih lanjut harus dievaluasi oleh dokter Anda.
- Sedang menjalani perawatan yang menekan sistem kekebalan tubuhnya (pertahanan alami tubuh) atau memiliki penyakit yang menyebabkan melemahnya sistem kekebalan tubuh. Dalam kasus ini respons imun terhadap vaksin mungkin akan menurun. Biasanya dianjurkan untuk menunggu sampai akhir pengobatan atau sembuhnya penyakit sebelum dilakukan vaksinasi. Akan tetapi anak-anak yang memiliki masalah jangka panjang dengan sistem kekebalan tubuh mereka seperti infeksi HIV (AIDS) masih dapat diberi HEXAXIM tetapi perlindungannya mungkin tidak sebagus pada anak-anak yang sistem kekebalan tubuhnya sehat.
- Menderita penyakit akut atau kronis termasuk ketidakmampuan atau gagal ginjal kronis (ketidakmampuan dari ginjal untuk berfungsi sebagaimana mestinya).
- Memiliki masalah dengan darah yang menyebabkan mudah memar atau pendarahan dalam waktu yang lama setelah tersayat kecil. Dokter akan menyarankan Anda apakah anak Anda perlu mendapatkan HEXAXIM.

Pingsan dapat terjadi setelah , atau bahkan sebelum, suntikan jarum apa pun. Oleh karena itu, beri tahu dokter atau perawat anak Anda pingsan dengan suntikan sebelumnya.

Obat lain atau vaksin dan HEXAXIM

Beritahukan kepada dokter atau perawat Anda jika anak Anda adalah sedang menggunakan obat tertentu, baru saja menggunakan atau dalam waktu dekat akan menggunakan obat atau vaksin lain.

HEXAXIM dapat diberikan pada saat bersamaan dengan vaksin lain seperti vaksin pneumokokus, vaksin campak-gondong-rubella atau vaksin rotavirus.

Data terkait penggunaan secara bersamaan Hexaxim dengan vaksin konjugat meningococcal C atau vaksin konjugat meningococcal kelompok A, C, W-135 dan Y menunjukkan tidak ada gangguan respon antibodi yang berarti untuk setiap antigen.

Studi jangka panjang mengenai kemampuan vaksin dalam menginduksi antibodi, baik dengan atau tanpa pemberian vaksin Hepatitis B pada masa kelahiran, telah menunjukkan kemampuan mempertahankan tingkat antibodi dalam tubuh di atas batas perlindungan atau pada ambang batas antigen vaksin. Imunitas terhadap komponen Hepatitis B yang terdapat dalam vaksin telah terbukti mampu bertahan sampai usia 9 tahun setelah pemberian primer vaksin Hepatitis B pada kelahiran diikuti dengan 3 dosis seri pada usia 2, 4, dan 6 bulan tanpa booster.
Ketika diberikan pada saat yang bersamaan dengan vaksin lainnya, HEXAXIM akan diberikan di lokasi suntikan yang berbeda.

Hexaxim mengandung fenilalanin, kalium dan natrium

Hexaxim mengandung 85 mikrogram fenilalanin dalam setiap dosis 0,5 ml. Fenilalanin mungkin berbahaya jika Anda menderita fenilketonuria (PKU), kelainan genetik langka di mana fenilalanin menumpuk karena tubuh tidak dapat mengeluarkannya dengan benar.
Hexaxim mengandung kurang dari 1 mmol kalium (39 mg) dan kurang dari 1 mmol natrium (23 mg) per dosis, artinya pada dasarnya "bebas kalium" dan "bebas natrium".

3. Cara menggunakan HEXAXIM

HEXAXIM akan diberikan kepada anak Anda oleh dokter atau perawat yang terlatih dalam memberikan vaksin dan yang memiliki kemampuan untuk menangani berbagai reaksi alergi parah yang tidak lazim pada injeksi/suntikan (lihat bagian 4 kemungkinan efek samping).
HEXAXIM diberikan berupa suntikan pada otot (rute intramuscular IM) di bagian atas kaki atau lengan atas anak Anda. Vaksin ini tidak akan disuntikkan ke dalam pembuluh darah atau dalam atau di bawah kulit.
Dosis yang dianjurkan adalah sebagai berikut:
Pemberian vaksinasi pertama (vaksinasi primer)
Anak Anda akan mendapatkan tiga suntikan yang diberikan pada selang waktu satu hingga dua bulan (setidaknya berjarak empat minggu). Vaksin ini harus digunakan sesuai dengan program vaksinasi lokal.
Suntikan tambahan (*booster*)
Setelah pemberian suntikan pertama, anak Anda akan mendapatkan dosis booster, sesuai dengan rekomendasi lokal, setidaknya 6 bulan setelah dosis terakhir dari pemberian pertama. Dokter akan memberitahu Anda ketika dosis ini harus diberikan.

Jika Anda lupa satu kali dosis HEXAXIM

Jika anak Anda melewatkan suntikan vaksin yang dijadwalkan, merupakan hal yang penting bagi Anda untuk mengkonsultasikan dengan dokter atau perawat mengenai siapa yang akan memutuskan kapan memberikan dosis yang terlewatkan.

Penting untuk selalu mengikuti petunjuk dari dokter atau perawat bahwa anak Anda harus menyelesaikan pemberian suntikan. Jika tidak, anak Anda mungkin tidak terlindungi sepenuhnya terhadap penyakit.

Jika Anda memiliki pertanyaan lebih lanjut tentang penggunaan vaksin ini, tanyakan kepada dokter, apoteker, atau perawat Anda.

4. Kemungkinan efek samping

Seperti semua obat-obatan, vaksin ini dapat menimbulkan efek samping, meskipun tidak semua orang mengalaminya.

Reaksi alergi yang serius (reaksi anafilaksis):

Jika gejala-gejala berikut ini terjadi setelah anak Anda mendapatkan suntikan vaksinnya, Anda harus berkonsultasi dengan dokter SEGERA:

- Sulit bernapas
- Lidah atau bibir menjadi biru
- Ruam
- Pembengkakan wajah atau tenggorokan
- Tekanan darah rendah sehingga menyebabkan pusing atau pingsan.

Ketika tanda-tanda atau gejala-gejala ini muncul, gejala atau tanda tersebut biasanya berkembang dengan cepat setelah suntikan dilakukan dan saat anak masih di klinik atau dokter bedah.

Reaksi alergi yang serius merupakan kemungkinan yang sangat langka (mungkin mempengaruhi 1 dari 10.000 orang) setelah menerima vaksin tertentu.

Efek samping lain:

Jika anak Anda mengalami salah satu dari efek samping berikut, mohon hubungi dokter, perawat, atau apoteker Anda.

- Efek samping sangat umum (dapat mempengaruhi lebih dari 1 dari 10 orang) adalah:
    - Kehilangan nafsu makan (anoreksia)

- Menangis
- Mengantuk (somnolen)
- Muntah
- Nyeri, kemerahan atau bengkak di tempat suntikan
- Mudah marah
- Demam (suhu 38ºC atau lebih tinggi)

- Efek samping umum (mungkin mempengaruhi hingga 1 di antara 10 orang) yaitu:
  - Menangis dengan tidak wajar (menangis berkepanjangan)
  - Diare
  - Terjadi pengerasan di tempat suntikan (indurasi)
- Efek samping yang tidak umum terjadi (mungkin mempengaruhi hingga 1 diantara 100 orang) yaitu:
  - Reaksi alergi
  - Benjolan (nodul) di tempat suntikan
  - Demam tinggi (suhu 39,6ºC atau lebih)
- Efek samping yang jarang terjadi (dapat mempengaruhi hingga 1 diantara 1.000 orang) yaitu:
  - Ruam
  - Reaksi meluas di tempat suntikan (lebih besar dari 5 cm), termasuk pembengkakan anggota tubuh yang meluas dari tempat suntikan lebih pada satu atau kedua sendi. Reaksi ini mulai terjadi dalam waktu 24-72 jam setelah vaksinasi, dapat dikaitkan dengan kemerahan, hangat, nyeri atau sakit di tempat suntikan, dan akan membaik dalam waktu 3-5 hari tanpa perlu pengobatan.
- Efek samping yang sangat jarang terjadi (mungkin hanya mempengaruhi hingga 1 diantara 10.000 orang) yaitu:
  - Episode ketika anak Anda mulai berada dalam kondisi seperti syok atau pucat, sangat lemas, dan tidak responsif untuk beberapa waktu (reaksi hiponotik atau episode hipotonik hiporesponsif HHE).

Potensi efek samping

Efek samping lain yang tidak tercantum di bagian di atas telah dilaporkan kadang-kadang terjadi pada pemberian vaksin dengan difteri, tetanus, pertussis, polio, hepatitis B atau vaksin yang mengandung Hib dan tidak langsung akibat dari HEXAXIM:

- Reaksi alergi yang serius (reaksi anafilaksis)
- Kejang demam atau kejang tanpa demam
- Peradangan sementara saraf yang menyebabkan nyeri, kelumpuhan, dan gangguan sensitivitas (sindrom Guillain-Barre) dan sakit parah dan penurunan mobilitas lengan dan bahu (neuritis brakial) telah dilaporkan setelah pemberian vaksin yang mengandung tetanus.
- Peradangan beberapa saraf yang menyebabkan gangguan sensor atau kelemahan anggota badan (Poliradikuloneuritis), kelumpuhan wajah, gangguan penglihatan, mendadak berkurang atau kehilangan daya penglihatan (Neuritis optik), Penyakit radang otak dan sumsum tulang belakang (demielinasi sistem saraf pusat, sklerosis ganda) telah dilaporkan setelah pemberian vaksin yang mengandung antigen hepatitis B.
- Pembengkakan atau radang otak (ensefalopati / ensefalitis).
- Pada bayi yang lahir sangat premature (tepat atau sebelum 28 minggu kehamilan jarak yang lebih lama di antara pernapasan normal dapat terjadi selama 2-3 hari setelah vaksinasi.
- Terjadi pembengkakan pada satu atau kedua kaki dan anggota badan bawah yang mungkin disertai dengan perubahan warna kebiruan pada kulit (sianosis), kemerahan, pendarahan pada daerah kecil di bawah kulit (purpura trasien) dan menangis dengan hebat setelah mendapatkan vaksinasi yang mengandung Haemophillus influenzae tibe b. Jika reaksi ini terjadi, biasanya terutama setelah suntikan pertama dan dalam beberapa jam pertama setelah vaksinasi. Semua gejala akan hilang sepenuhnya dalam waktu 24 jam tanpa perlu pengobatan.
- Jika anak Anda mendapatkan efek samping, bicarakan dengan dokter, apoteker, atau perawat Anda. Efek tersebut mungkin meliputi efek samping tidak terdapat dalam leaflet ini.

Pelaporan efek samping

Jika Anda atau anak Anda mendapatkan efek samping, bicarakanlah dengan dokter, apoteker atau

perawat Anda. Termasuk kemungkinan efek samping yang tidak tercantum dalam brosur ini.
Anda juga dapat melaporkan efek samping secara langsung ke Industri Farmasi dengan kontak berikut farmakovigilans@kalventis.com.
Dengan melaporkan efek samping Anda dapat membantu memberikan informasi tentang keamanan obat ini.

Overdosis

Belum ada kasus overdosis yang dilaporkan.

5. Cara menyimpan HEXAXIM

Jauhkan vaksin dari pandangan dan jangkauan anak-anak.

Jangan gunakan vaksin ini setelah tanggal kadaluwarsa yang tertera di karton dan label setelah EXP. Tanggal kadaluarsa itu mengacu pada hari terakhir pada bulan itu.

Simpan di lemari es (dengan suhu 2ºC - 8ºC).

Jangan dibekukan.

Usahakan agar tetap vaksin dalam karton pelindung untuk melindunginya dari cahaya.

Data kestabilan Hexaxim mengindikasikan bahwa komponen vaksin stabil pada suhu sampai 25°C selama 72 jam. Di akhir periode ini, Hexaxim sebaiknya digunakan atau dibuang.

Jangan membuang obat di saluran limbah atau pembuangan sampah rumah tangga. Tanyakan kepada apoteker Anda bagaimana membuang obat yang tidak Anda gunakan lagi. Langkah-langkah tersebut akan membantu menjaga lingkungan.

6. Isi paket dan informasi-informasi lainnya

Apakah kandungan HEXAXIM

Zat aktif per dosis (0.5 ml)[1]:

Toksoid Difteri	tidak kurang dari 20 IU[2,4] (30 Lf)
Toksoid Tetanus	tidak kurang dari 40 IU[3,4] (10 Lf)
Antigen *Bordetella pertussis*	
Toksoid Pertussis	25 mikrogram
Haemagglutinin Filamen Virus	25 mikrogram
polio (dilemahkan)[5]	
Tipe 1 (Mahoney)	29 D unit antigen[6]
Tipe 2 (MEF-1)	7 D unit antigen[6]
Tipe 3 (Saukett)	26 D antigen unit[6]
Antigen permukaan Hepatitis B[7]	10 mikrogram
Polisakarida *Haemophilus influenzae* tipe b	12 mikrogram
(Fosfat *Polyribosylribitol*)	
Protein Tetanus terkonjugasi	22-36 mikrogram

[1]*Terjerap (adsorbed) pada aluminium hidroksida, terhidrasi (0,6 mg Al^{3+})*

[2]*Sebagai lower confidence limit (p=0.95) dan nilai rata-rata tidak kurang dari 30 IU*

[3]*Sebagai lower confidence limit (p=0.95)*

[4]*Atau aktivitas setara yang ditentukan oleh evaluasi imunogenisitas*

[5]*Dibudidayakan pada sel Vero*

[6]*Jumlah antigen ini benar-benar sama dengan yang sebelumnya dinyatakan sebagai unit antigen D 40-8-32, masing-masing untuk virus tipe 1,2, dan 3, bila diukur dengan metode imunokimia lain yang sesuai*

[7]*Diproduksi dalam sel khamir (yeast) Hansenula polymorpha dengan teknologi DNA rekombinan*

Bahan-bahan lain yaitu:

Dinatrium hydrogen fosfat, kalium dihidrogen fosfat, trometamol, sukrosa, asam amino esensial meliputi L-fenilalanina, natrium hidroksida, asam asetat atau asam klorida (untuk penyesuaian pH) dan air untuk suntikan.

Vaksin tersebut mungkin mengandung runutan (trace) glutaraldehid, formaldehid, neomisin, streptomisin dan polimiksin B.

Seperti apa HEXAXIM itu dan apa isi paketnya

HEXAXIM disediakan sebagai suspensi untuk suntikan dalam bentuk prefilled syringe (0,5 ml). HEXAXIM tersedia dalam paket berisi 1 prefilled syringe yang berisi 0,5 mL dengan 2 jarum terpisah.

Setelah dikocok, tampilan normal vaksin ini berupa suspensi keputihan keruh.

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No. Reg: DKI1459703243A1

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi

HARUS DENGAN RESEP DOKTER

sanofi

Berdasarkan persetujuan BPOM tanggal XXX – Luer-Lock, CCDSv14, and Standar Informasi Obat