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)

Read all of this leaflet carefully before your child is vaccinated because it contains important information for him/her.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If your child gets any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What HEXAXIM is and what it is used for

HEXAXIM (DTaP-IPV-HB-Hib) is a vaccine used to protect against infectious diseases.

HEXAXIM helps to protect against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and serious diseases caused by *Haemophilus influenzae* type b. HEXAXIM is given to children from six weeks of age.

The vaccine works by causing the body to produce its own protection (antibodies) against the bacteria and viruses that cause these different infections:

- Diphtheria is an infectious disease that usually first affects the throat. In the throat, the infection causes pain and swelling which can lead to suffocation. The bacteria that cause the disease also make a toxin (poison) that can damage the heart, kidneys and nerves.
- Tetanus (often called lock jaw) is usually caused by the tetanus bacteria entering a deep wound. The bacteria make a toxin (poison) that causes spasms of the muscles, leading to inability to breathe and the possibility of suffocation.
- Pertussis (often called whooping cough) is a highly infectious illness that affects the airways. It causes severe coughing that may lead to problems with breathing. The coughing often has a "whooping" sound. The cough may last for one to two months or longer. Whooping cough can also cause ear infections, chest infections (bronchitis) which may last a long time, lung infections (pneumonia), fits, brain damage and even death.
- Hepatitis B is caused by the hepatitis B virus. It causes the liver to become swollen (inflamed). In some people, the virus can stay in the body for a long time, and can eventually lead to serious liver problems, including liver cancer.
- Poliomyelitis (often just called polio) is caused by viruses that affect the nerves. It can lead to paralysis or muscle weakness most commonly of the legs. Paralysis of the muscles that control breathing and swallowing can be fatal.
- *Haemophilus influenzae* type b infections (often just called Hib) are serious bacterial infections and can cause meningitis (inflammation of the outer covering of the brain), which can lead to brain damage, deafness, epilepsy, or partial blindness. Infection can also cause inflammation and swelling of the throat, leading to difficulties in swallowing and breathing, and infection can

affect other parts of the body such as the blood, lungs, skin, bones, and joints.

Important information about the protection provided

- HEXAXIM will only help to prevent these diseases if they are caused by the bacteria or viruses targeted by the vaccine. Your child could get diseases with similar symptoms if they are caused by other bacteria or viruses.
- The vaccine does not contain any live bacteria or viruses and it cannot cause any of the infectious diseases against which it protects.
- This vaccine does not protect against infections caused by other types of *Haemophilus influenzae* nor against meningitis due to other micro-organisms.
- HEXAXIM will not protect against hepatitis infection caused by other agents such as hepatitis A, hepatitis C and hepatitis E.
- Because symptoms of hepatitis B take a long time to develop, 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.
- As with any vaccine, HEXAXIM may not protect 100% of children who receive the vaccine.

2. What you need to know before HEXAXIM is given to your child

To make sure that HEXAXIM is suitable for your child, it is important to talk to your doctor or nurse if any of the points below apply to your child. If there is anything you do not understand, ask your doctor, pharmacist or nurse to explain.

Do not use HEXAXIM if your child:

- has had respiratory disorder or swelling of the face (anaphylactic reaction) after administration of HEXAXIM.
- has had an allergic reaction
  - to the active substances,
  - to any of the excipients listed in section 6,
  - to glutaraldehyde, formaldehyde, neomycin, streptomycin or polymyxin B, as these substances are used during the manufacturing process,
  - after previous administration of HEXAXIM or any other diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B or Hib containing vaccines.
- suffered from a severe reaction affecting the brain (encephalopathy) within 7 days of a prior dose of a pertussis vaccine (acellular or whole cell pertussis).
- has an uncontrolled condition or severe illness affecting the brain and nervous system (uncontrolled neurologic disorder) or uncontrolled epilepsy.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before vaccination if your child:

- has a moderate or high temperature or an acute illness (e.g. fever, sore throat, cough, cold or flu). Vaccination with HEXAXIM may need to be delayed until your child is better.
- has had any of the following events after receiving a pertussis vaccine, as the decision to give further doses of pertussis containing vaccine will need to be carefully considered:
  - fever of 40°C or above within 48 hours of vaccination not due to another identifiable cause.
  - collapse or shock-like state with hypotonic-hyporesponsive episode (drop in energy) within 48 hours of vaccination.
  - persistent, inconsolable crying lasting 3 hours or more, occurring within 48 hours of vaccination.
  - fits (convulsions) with or without fever, occurring within 3 days of vaccination.
- previously had Guillain-Barré syndrome (temporary inflammation of nerves causing pain, paralysis and sensitivity disorders) or brachial neuritis (severe pain and decreased mobility of arm and shoulder) after being given a vaccine containing tetanus toxoid (an inactivated form of

tetanus toxin). In this case, the decision to give any further vaccine containing tetanus toxoid should be evaluated by your doctor.
- is having a treatment that suppresses her/his immune system (the body's natural defenses) or has any disease that causes the weakness of the immune system. In these cases the immune response to the vaccine may be decreased. It is normally recommended to wait until the end of the treatment or disease before vaccinating. However children with long standing problems with their immune system such as HIV infection (AIDS) may still be given HEXAXIM but the protection may not be as good as in children whose immune system is healthy.
- suffers from an acute or chronic illness including chronic renal insufficiency or failure (inability of the kidneys to work properly).
- suffers from any undiagnosed illness of the brain or epilepsy which is not controlled. Your doctor will assess the potential benefit offered by vaccination.
- has any problems with the blood that cause easy bruising or bleeding for a long time after minor cuts. Your doctor will advise you whether your child should have HEXAXIM.

Fainting can occur following, or even before, any needle injection. Therefore, tell your doctor or nurse your child fainted with a previous injection.

Other medicines or vaccines and HEXAXIM
Tell your doctor or nurse if your child is taking, has recently taken or might take any other medicines or vaccines.
HEXAXIM can be given at the same time as other vaccines such as pneumococcal vaccines, measles-mumps-rubella vaccines, rotavirus vaccines or meningococcal vaccines.
When given at the same time with other vaccines, HEXAXIM will be given at different injection sites.

HEXAXIM contains phenylalanine, potassium and sodium

HEXAXIM contains 85 micrograms phenylalanine in each 0.5 ml dose. Phenylalanine may be harmful if you have 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".

3. How to use HEXAXIM

HEXAXIM will be given to your child by a doctor or nurse trained in the use of vaccines and who are equipped to deal with any uncommon severe allergic reaction to the injection (see section 4 Possible side effects).
HEXAXIM is given as an injection into a muscle (intramuscular route IM) in the upper part of your child's leg or upper arm. The vaccine will never be given into a blood vessel or into or under the skin.

The recommended dose is as follows:

First course of vaccination (primary vaccination)
Your child will receive either two injections given at an interval of two months or three injections given at an interval of one to two months (at least four weeks apart). This vaccine should be used according to the local vaccination programme.

Additional injections (booster)
After the first course of injections, your child will receive a booster dose, in accordance with local recommendations, at least 6 months after the last dose of the first course. Your doctor will tell you when this dose should be given.

If you forget one dose of HEXAXIM
If your child misses a scheduled injection, it is important that you discuss with your doctor or nurse who will decide when to give the missed dose.

It is important to follow the instructions from the doctor or nurse so that your child completes the course of injections. If not, your child may not be fully protected against the diseases.

If you have any further questions on the use of this vaccine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

Serious allergic reactions (anaphylactic reaction)
If any of these symptoms occur after leaving the place where your child received his/her injection, you must consult a doctor IMMEDIATELY:

- difficulty in breathing
- blueness of the tongue or lips
- a rash
- swelling of the face or throat
- sudden and serious malaise with drop in blood pressure causing dizziness and loss of consciousness, accelerated heart rate associated with respiratory disorders.

When these signs or symptoms (signs or symptoms of anaphylactic reaction) occur they usually develop quickly after the injection is given and while the child is still in the clinic or doctor's surgery.

Serious allergic reactions are a rare possibility (may affect up to 1 in 1,000 people) after receiving this vaccine.

Other side effects
If your child experiences any of the following side effects, please tell your doctor, nurse or pharmacist.

- Very common side effects (may affect more than 1 in 10 people) are:
  - loss of appetite (anorexia)
  - crying
  - sleepiness (somnolence)
  - vomiting
  - pain, redness or swelling at the injection site
  - irritability
  - fever (temperature 38°C or higher)
- Common side effects (may affect up to 1 in 10 people) are:
  - abnormal crying (prolonged crying)
  - diarrhoea
  - injection site hardness (induration)
- Uncommon side effects (may affect up to 1 in 100 people) are:
  - allergic reaction
  - lump (nodule) at the injection site
  - high fever (temperature 39.6°C or higher)
- Rare side effects (may affect up to 1 in 1,000 people) are:
  - rash
  - large reactions at the injection site (larger than 5 cm), including extensive limb swelling from the injection site beyond one or both joints. These reactions start within 24-72 hours after vaccination, may be associated with redness, warmth, tenderness or pain at the injection site, and get better within 3-5 days without the need for treatment.
  - fits (convulsions) with or without fever.
- Very rare side effects (may affect up to 1 in 10,000 people) are:
  - episodes when your child goes into a shock-like state or is pale, floppy and unresponsive for a period of time (hypotonic reactions or hypotonic hyporesponsive episodes HHE).

Potential side effects
Other side effects not listed above have been reported occasionally with other diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B or Hib containing vaccines and not directly with HEXAXIM:

- Temporary inflammation of nerves causing pain, paralysis and sensitivity disorders (Guillain-Barré syndrome) and severe pain and decreased mobility of arm and shoulder (brachial neuritis) have been reported after administration of a tetanus containing vaccine.
- Inflammation of several nerves causing sensory disorders or weakness of limbs (polyradiculoneuritis), facial paralysis, visual disturbances, sudden dimming or loss of vision (optic neuritis), inflammatory disease of brain and spinal cord (central nervous system demyelination, multiple sclerosis) have been reported after administration of a hepatitis B antigen containing vaccine.
- Swelling or inflammation of the brain (encephalopathy/encephalitis).
- In babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2 - 3 days after vaccination.
- Swelling of one or both feet and lower limbs which may occur along with bluish discoloration of the skin (cyanosis), redness, small areas of bleeding under the skin (transient purpura) and severe crying following vaccination with *Haemophilus influenzae* type b containing vaccines. If this reaction occurs, it is mainly after first injections and within the first few hours following vaccination. All symptoms should disappear completely within 24 hours without need for treatment.

Reporting of side effects
If your child gets any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store HEXAXIM

Keep this vaccine out of the sight and reach of children.
Do not use this vaccine after the expiry date which is stated on the carton and the label after EXP. The expiry date refers to the last day of that month.
Store in a refrigerator (2°C - 8°C).
Do not freeze.
Keep the vaccine in the outer carton in order to protect from light.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What HEXAXIM contains
The active substances are per dose (0.5 ml)[1]:

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] *IU International Unit*
[3] *Or equivalent activity determined by an immunogenicity evaluation*
[4] *Produced on Vero cells*
[5] *Equivalent antigenic quantity in the vaccine*
[6] *Produced in yeast Hansenula polymorpha cells by recombinant DNA technology*

The other ingredients are:
Disodium hydrogen phosphate, potassium dihydrogen phosphate, trometamol, saccharose, essential amino acids including L-phenylalanine, sodium hydroxide and/or acetic acid and/or hydrochloric acid (for pH adjustment), and water for injections.

The vaccine may contain traces of glutaraldehyde, formaldehyde, neomycin, streptomycin and polymyxin B.

What HEXAXIM looks like and contents of the pack
HEXAXIM is provided as a suspension for injection in pre-filled syringe (0.5 ml).
HEXAXIM is available in pack containing 1 or 10 pre-filled syringes without attached needle.
HEXAXIM is available in pack containing 1 or 10 pre-filled syringes with 1 separate needle.
HEXAXIM is available in pack containing 1 or 10 pre-filled syringes with 2 separate needles.

Not all pack sizes may be marketed.

After shaking, the normal appearance of the vaccine is a whitish cloudy suspension.

Marketing Authorisation Holder
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The following information is intended for healthcare professionals only:

- For syringes without attached needle, the needle must be fitted firmly to the syringe, rotating it by a one-quarter turn.
- Shake the pre-filled syringe so that the contents become homogeneous.
- HEXAXIM should not be mixed with other medicinal products.
- HEXAXIM must be administered intramuscularly. 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).
  The intradermal or intravenous routes must not be used. Do not administer by intravascular injection: ensure that the needle does not penetrate a blood vessel.