For the use of Registered Medical Practitioner or Hospital or Laboratory only.

Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA), *Haemophilus influenzae* Type b Conjugate and Poliomyelitis (Inactivated) Vaccine (Adsorbed)

Shan6™

COMPOSITION

Shan6™ is an adsorbed hexavalent liquid combination vaccine composed of Diphtheria Toxoid, Tetanus Toxoid, *Bordetella pertussis* (whole cell), Hepatitis B surface antigen (rDNA), *Haemophilus influenzae* type b purified capsular polysaccharide conjugated to Tetanus Toxoid, and Poliomyelitis virus (Inactivated) to be administered by the intramuscular route.

The vaccine meets the WHO/In-house requirements for manufacture of biological substances.

Active Ingredients	Quantity per 0.5-mL single dose^
Diphtheria Toxoid	≥30 IU[$]
Tetanus Toxoid	≥60 IU[$]
Bordetella pertussis (Whole Cell inactivated)	≥4 IU
rDNA Hepatitis B Surface Antigen	10 µg[$]
Haemophilus influenzae type b polysaccharide (Polyribosylribitol Phosphate) conjugated to tetanus toxoid 22 to 40 µg	12 µg[¶]
Poliomyelitis virus (Inactivated) Type 1 (Mahoney Strain)[#] Type 2 (MEF-1 Strain)[#] Type 3 (Saukett Strain)[#]	 29 DU[*] 7 DU[*] 26 DU[*]
Excipients	
Aluminium Phosphate Gel equivalent to Al[+++]	0.625 mg
Sodium Chloride	4.5 mg
Water for Injections	q.s. to 0.5 mL
^Multi-dose vial contains preservatives: 2-phenoxyethanol[£] (0.6% v/v) and formaldehyde (6.25 µg)	

[$]The lower confidence limit (P = 0.95)
[$]Produced in yeast *Hansenula polymorpha* cells by recombinant DNA technology
[¶]Expressed as amount of polysaccharide
[#]Produced on VERO cells
[*] DU: D-antigen Unit
[£]2-phenoxyethanol contained in a solution of 2-phenoxyethanol at 50% in ethanol

The vaccine may contain traces of neomycin, streptomycin, polymyxin B, and essential amino acids including L-Phenylalanine.

DOSAGE FORM/S, INDICATIONS

Suspension for injection in multi-dose vial. **Shan6™** is a whitish turbid suspension in which the Aluminium Phosphate adjuvant tends to settle down slowly on storage.

Shan6™ is indicated for primary vaccination against diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, and invasive diseases caused by *Haemophilus influenzae* type b from the age of 6 weeks onwards, in accordance with official recommendations.

DOSAGE AND ADMINISTRATION

Dosage

Primary vaccination

The primary vaccination schedule consists of 3 doses of **Shan6™** injection (0.5 mL each) to be administered intramuscularly at an interval of at least 4 weeks in accordance with official recommendations.

Shan6™ can be used whether or not a dose of Hepatitis B vaccine has been given at birth.

Administration

Shan6™ must be administered intramuscularly only. The recommended injection site is generally the anterolateral aspect of the upper thigh in infants and toddlers. Do not administer via intravascular route: ensure that the needle does not penetrate a blood vessel. Separate syringes, separate injection sites, and preferably separate limbs must be used in case of concomitant administration with other vaccines.

USE IN SPECIAL POPULATIONS

Pregnancy and Lactation: Shan6™ is intended for use in pediatric populations.

Pediatric patients: The safety and efficacy of **Shan6™** in infants younger than 6 weeks of age have not been established. No data are available on the use of **Shan6™** in children aged between 24 months and younger than 7 years.

In children younger than 7 years of age, if vaccinations are missed, the next dose should be given, regardless of the interval since last dose as long as it is ≥4 weeks.

Fertility: Shan6™ is not intended for administration to individuals of fertility age.

CONTRAINDICATIONS

- History of severe allergic reaction to any component of the vaccine or to any pertussis vaccine, after previous administration of the vaccine or a vaccine containing the same components or constituents.
- History of encephalopathy within 7 days of administration of a previous dose of any vaccine containing pertussis antigens (whole cell or acellular pertussis vaccines).
- History of progressive neurologic disorder, uncontrolled epilepsy, or progressive encephalopathy. Pertussis vaccines should not be administered to individuals with these conditions until the treatment regimen has been established, the condition has stabilized, and the benefit estimated to clearly outweigh the risk.

WARNINGS AND PRECAUTIONS

Hypersensitivity

Caution should be exercised when **Shan6™** is administered to subjects with hypersensitivity to formaldehyde, neomycin, streptomycin and polymyxin B.

Protection

- **Shan6™** will not protect against hepatitis infection caused by other agents such as hepatitis A, hepatitis C, and hepatitis E viruses or by other liver pathogens.
- Because of the long incubation period of hepatitis B virus infection, it is possible for unrecognized hepatitis B infections to be present at the time of vaccination. The vaccine will not prevent hepatitis B infection in such cases.
- **Shan6™** does not protect against infectious diseases caused by other serotypes of *Haemophilus influenzae* or against meningitis of other origins.
- As with any vaccine, vaccination with **Shan6™** may not protect 100% of susceptible individuals against the target diseases.

Special patient groups

- The immunogenicity of the vaccine may be reduced by immunosuppressive treatments or immunodeficiency conditions. It is recommended to postpone vaccination until the end of such treatment or diseases. Nevertheless, vaccination of subjects with chronic immunodeficiency, such as untreated HIV infection, is recommended even if antibody responses to some vaccine antigens may be limited.
- No data are available for premature infants with **Shan6™**. Lower immune response may be observed in this population in relation with immaturity of the immune system. However, according to several national recommendations, vaccination should not be delayed.
- The potential risk of apnea and the need for cardio-respiratory monitoring for 48 to 72 hours should be considered when administering the primary immunization 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 chronic renal failure subjects, impaired hepatitis B vaccine response has been observed and administration of additional doses of hepatitis B vaccines should be considered according to the antibody level against hepatitis B virus surface antigen (anti-HBsAg).
- If Guillain-Barre syndrome has occurred following the 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 immunization schedule has been completed. Official recommendations should be followed to assess whether vaccination is justified in such circumstances.

Precautions

- Do not administer by intravascular injection.
- Vaccination should be postponed in children suffering from moderate-to-severe acute febrile illness or infection and until resolution. The presence of a minor infection and/or low-grade fever should not result in the deferral of vaccination.
- As with all injectable vaccines, the vaccine must be administered with caution to subjects with thrombocytopenia or a bleeding disorder because bleeding may occur following an intramuscular administration.
- As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.
- If any of the following events are known to have occurred in temporal relation to receipt of one pertussis-containing vaccine, the decision to give further doses of one pertussis-containing vaccine should be carefully considered:
  - Temperature of ≥40°C within 48 hours not due to another identifiable cause.
  - Collapse or shock-like state (Hypotonic Hyporesponsive Episodes) 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.

DRUG INTERACTIONS

Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA), *Haemophilus influenzae* Type b Conjugate and Poliomyelitis (Inactivated) vaccines are expected not to interfere with OPV, Measles vaccine,Measles Mumps Rubella (MMR) vaccine and Oral Rotavirus Vaccine (ORV).

Data on concomitant administration of **Shan6™** with ORVs have shown no clinically relevant interferences on the antibody responses to each of the individual vaccine antigens when given as a 3-dose primary vaccination.

Except in the case of immunosuppressive therapy (See WARNINGS AND PRECAUTIONS), no significant clinical interaction with other treatments or biological products has been reported.

ADVERSE REACTIONS

The following CIOMS frequency rating is used.

Very common: ≥10%
Common: ≥1 and <10%
Uncommon: ≥0.1 and <1%
Rare: ≥0.01 and <0.1%
Very rare: <0.01%
Not known: cannot be estimated from available data

Adverse event information is derived from clinical trials with Shan6™.

Clinical Trials

The safety of **Shan6™** in infants was assessed in two randomized, controlled clinical trials in which 1059 infants aged 6 to 8 weeks, 10 to 12 weeks, and 14 to 16 weeks received 3 doses (0.5-mL) of **Shan6™** in primary series. For all subjects, safety evaluations were performed during the first 28 days following each vaccination.

Most of reactions usually occurred within the first 3 days following vaccination and resolved spontaneously within 1 to 3 days after onset. The intensity of these reactions was mild to moderate. In the primary series, reactions were observed to be more frequent after the first dose and less frequent after the subsequent doses.

Primary series (3 doses with 4 weeks apart) involving 1059 Infants (starting at 6 weeks of age).

Very commonly observed reactions were injection-site pain, injection-site erythema, injection-site swelling, pyrexia, vomiting, crying, somnolence, decreased appetite, and irritability. The reactions were observed to be more frequent after the first dose and less frequent after the subsequent doses.

Uncommon: Injection-site nodule, Injection site induration

Potential Adverse Events

Adverse events that have been reported with other vaccines containing one or more of the components or constituents of **Shan6™** and not directly with **Shan6™**.

- Encephalopathy/encephalitis
- Hypotonic Hyporesponsive Episodes
- Convulsions
- 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 to 72 hours after vaccination; may be associated with erythema, warmth, tenderness, or pain at the injection site; and resolve spontaneously within 3 to 5 days. The risk appears to be dependent on the number of prior doses, with a greater risk following the 4th and 5th doses.
- 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.

OVERDOSE

Not documented.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics properties:

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

Immunogenicity

In pivotal Phase III study (SH600003), the seroprotection rates 28 days after primary vaccination (3 doses) were at 100% for diphtheria, tetanus, *Haemophilus influenzae* type b, types 1 and type 3 of polioviruses and at 99.7% for hepatitis B and type 2 of poliovirus. For pertussis, the vaccine response rates were at 84.3% for anti-pertussis toxin (PT), 97.7% for anti-fimbriae (FIM), 75% for anti- filamentous hemagglutinin (FHA) and 85.1% for anti-pertactin (PRN) antibodies.

Pharmacokinetic properties

Not applicable.

INCOMPATIBILITIES

Shan6™ must not be mixed with other vaccines or other parenterally administered drugs.

SHELF-LIFE

The shelf life is 30 months.

PACKAGING INFORMATION

Multi dose vial (10 doses) 5.0 mL

Shan6™ is presented in USP type I glass vial with a Bromobutyl rubber stopper and Aluminium flip-Off seal.

STORAGE AND HANDLING INSTRUCTIONS

Keep vaccine out of the sight and reach of children.

Do not use vaccine after the expiry date which is stated on the carton and the label.

Store in a refrigerator (+2°C to +8°C). Do not freeze. Discard vaccine if frozen.

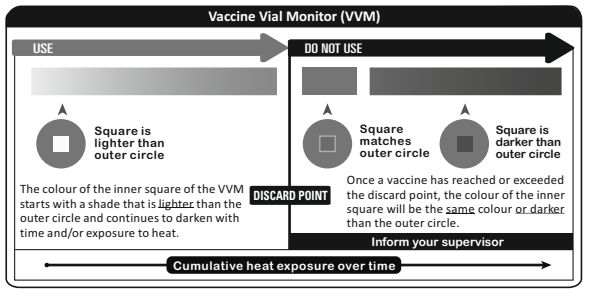
Vaccine should be protected from light.

Before use, the vaccine should be shaken in order to obtain a homogeneous whitish turbid suspension.

For a multi-dose vial, after first opening, the vaccine can be used for up to 28 days, provided it is stored between +2°C to +8°C.

After use, any remaining vaccine and container must be disposed of safely, preferably by heat inactivation or incineration, according to locally agreed procedures.

The Vaccine Vial Monitors (VVM) are on the label of **Shan6™** vaccine supplied through Sanofi Healthcare India Private Limited. The colour dot which appears on the label of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.



The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the circle, then the vaccine can be used. As soon as the colour of the central square is the same colour as the circle or of a darker colour than the circle, then the vial should be discarded.

Manufactured & Marketed by:
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