1 Name of the medicinal product: Shan 5

2 Generic name: Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA) and Haemophilus influenzae Type b Conjugate Vaccine (Adsorbed).

3 Qualitative and Quantitative Composition:

Each dose of 0.5 mL contains:

<table>
<thead>
<tr>
<th>Active Ingredients</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria Toxoid</td>
<td>≥ 30 IU</td>
</tr>
<tr>
<td>Tetanus Toxoid</td>
<td>≥ 60 IU</td>
</tr>
<tr>
<td>B. pertussis (Whole cell)</td>
<td>≥ 4 IU</td>
</tr>
<tr>
<td>Hepatitis B Surface Antigen (rDNA)</td>
<td>10 µg</td>
</tr>
<tr>
<td>Purified capsular polysaccharide of Hib conjugated to 20 – 40 mcg of Tetanus Toxoid (carrier protein)</td>
<td>10 µg</td>
</tr>
</tbody>
</table>

For excipients, see Section 7.1.

4 Pharmaceutical form:

Presented as suspension for Intramuscular Injection.

5 Clinical Particulars:

5.1 Therapeutic Indication:

Shan 5 is indicated for active immunization against Diphtheria, Tetanus, Pertussis, Hepatitis B and Haemophilus influenzae type b in infants starting from 6-8 weeks of age. The vaccine should not be used as a birth dose vaccine.

5.2 Posology and Method of administration:

The recommended single human dose of the vaccine is 0.5 mL. The primary vaccination schedule consists of three doses administered at an interval of at-least 4 weeks between doses and starting at 6-8 weeks of age. In geographical areas where there is a high endemicity of Hepatitis B and significant perinatal transmission, the practice to administer monovalent Hepatitis B vaccine at birth should be continued. Three doses of the pentavalent vaccine can be used to complete the primary series starting from 6-8 weeks of age.

The liquid vaccine in the vial should be shaken before use to homogenize the suspension. The vaccine should be injected deep intramuscularly. Do not inject subcutaneously or intravenously. The anterolateral aspect of the upper thigh is the preferred site of injection. An injection into a child's buttocks may cause injury to the sciatic nerve and is not recommended. The vaccine must not be injected into the skin as this may give rise to local reactions. A sterile syringe and sterile needle must be used for the injection. Another
injectable vaccine if co-administered with Shan 5 should be administered at a different anatomical site. The vaccine should be visually inspected for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed discard the vaccine. Shan 5 should not be mixed with any other vaccine or injectable in the same syringe before administration.

Once opened multi-dose vials should be kept between +2°C and +8°C. Multi-dose vials of Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA) and Haemophilus influenzae Type b Conjugate Vaccine (Adsorbed) from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 4 weeks, provided that all of the following conditions are met:

- The expiry date has not passed.
- The vaccines are stored under appropriate cold chain conditions.
- The vaccine vial septum has not been submerged in water.
- Aseptic technique has been used to withdrawal doses.

5.3 Contraindications:

Shan 5 should not be administered to subjects with either known hypersensitivity to any component of the vaccine, or having shown signs of hypersensitivity after previous administration of Shan 5 or Diphtheria, Tetanus, Pertussis, Hepatitis B or Hib vaccines. It is a contraindication to administer the vaccine in the presence of any evolving or suspected neurological condition.

As with other vaccines, the administration of Shan 5 should be postponed in subjects suffering from acute severe febrile illness. However, the presence of minor illnesses such as mild upper respiratory infections with or without low grade fever is not a contraindication for further use.

Shan 5 is contra-indicated if the child has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis containing vaccine or any progressive neurological disorder. In these circumstances the vaccination may be continued with DT, Hib and Hepatitis B vaccines after a thorough medical evaluation and assessment of risk benefit.

5.4 Warnings and special precautions:

Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and the possible occurrence of undesirable events) and a clinical examination.

If any of the following events occur in temporal relation to receipt of Shan 5, the decision to give subsequent doses of Shan 5 or any other vaccine containing the pertussis component should be carefully considered.
• Temperature of $\geq 39.5^\circ\text{C} (103.1^\circ\text{F})$ within 48 hours, not due to another identifiable cause;
• Inconsolable crying lasting $\geq 3$ hours, occurring within 48 hours;
• Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours;
• Convulsions/Seizures with or without fever, occurring within 3 days.

There may be circumstances, such as presence of high fever, when the potential benefits of the vaccine use outweigh possible risks.

HIV infection is not considered as a contraindication for Diphtheria, Tetanus, Pertussis, Hib and Hepatitis B vaccination. The expected immunological response may not be obtained after vaccination of immunosuppressed patients, for example, patients on immunosuppressive therapy including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses). Vaccine should be administered to prevent the child from contacting the diseases and vaccination should be undertaken as per recommended standard schedules.

As with all injectable vaccines, appropriate medical treatment should always be readily available in case of anaphylactic reactions following the administration of the vaccine. For this reason, the vaccinee should remain under medical supervision for at-least 30 minutes after vaccination. Adrenaline injection (1:1000) must be immediately available should an acute anaphylactic reaction occur due to any component of the vaccine. For treatment of severe anaphylaxis the initial dose of adrenaline is 0.1 - 0.5 mg (0.1 - 0.5 mL of 1:1000 injection) given subcutaneously or intramuscularly. For infants the recommended dose of adrenaline is 0.01 mg/kg (0.01 mL/kg of 1:1000 injection). Single pediatric dose should not be more than 0.5 mg (0.5 mL). Post vaccination with injectable vaccines, it is expected that there may be minor swelling, tenderness and redness at the injection site. In case this does not resolve within seven days or if associated with any increase in severity, it should be brought to the physician’s notice immediately for further treatment and care.

Injectable vaccines should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects, unless the potential benefit clearly outweighs the risk of administration.

5.5 Special Populations:

Shan 5 is not indicated for use in pregnant women or in geriatric populations. Since the components of Shan 5 are either subunit, toxoids or killed whole cell bacteria, theoretically there is no increased risk in patients with HIV/AIDS however the expected immunological response may not be obtained after vaccination of immunosuppressed or immunologically compromised patients.
5.6 Interaction with other medicinal products and other forms of interaction:

DTwP-HepB-Hib vaccines are generally expected not to interfere with Polio vaccine (OPV & IPV), measles vaccine, MMR vaccine, BCG vaccine, Oral Rotavirus vaccine and Pneumococcal vaccines. A three dose primary series of the DTwP-HepB-Hib vaccines can be generally followed by measles, MMR, polio or DTP-Hib/DTP-HepB-Hib vaccines administered in later months as booster doses.

The vaccine should not be mixed in the same vials or syringes with another vaccine. As with other vaccine, it may be expected that in patients receiving immunosuppressive therapy, an adequate response may not be achieved.

5.7 Pregnancy and Lactation:

Shan 5 is not intended for use in adults.

5.8 Undesirable effects:

5.8.1 Summary of safety profile. The safety profile presented below is based on data generated in a clinical study. In the subjects who received Shan 5, the most frequently reported reactions included injection-site tenderness, erythema, mild swelling, fever, vomiting, excessive crying, drowsiness, appetite lost and irritability. Data are categorized by MedDRA system organ class.

5.8.2 Tabulated list of adverse reactions: The adverse events are ranked under headings of frequency per dose, using the following convention:

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

Metabolism and nutrition disorders

Very common: Appetite lost

Nervous system disorders

Very common: Drowsiness, Abnormal Crying (prolonged), Irritability.

Gastrointestinal disorders

Very Common: Vomiting

Skin and Subcutaneous disorders

Uncommon: Rash

General disorders and administration site conditions

Very common: Injection site tenderness, injection site erythema, fever ≥ 38°C, local swelling at the injection site (≤ 50 mm)

Uncommon: local swelling at the injection site (> 50 mm), including induration

These reactions start within 24 - 72 hrs after vaccination and resolved spontaneously within 3-5 days.
5.8.3 Potential Adverse Events: (i.e. adverse events which have been reported with other vaccines containing one or more of the components or constituents of Shan5 and not directly with Shan5). Brachial neuritis and Guillain-Barre Syndrome have been reported after administration of a Tetanus Toxoid containing vaccine. Oedematous reaction affecting one or both lower limbs may occur following vaccination with *Haemophilus influenzae* type b containing vaccines. If the reaction occurs it does show mainly after primary injections and is observed within the first few hours following vaccination. Associated symptoms may include cyanosis, redness, transient purpura and severe crying. All events resolve spontaneously without sequelae within 24 hours. Convulsion with or without fever, 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. Hypotonic-hyporesponsive episodes have been observed with whole cell pertussis component containing vaccine.

5.9 Effect on ability to drive and use machines:

Shan 5 is not intended for use in adults. Vaccines are expected induce antibody generation in the body which is not expected to have any undesirable effect on the ability of individuals to drive or use machines.

5.10 Overdose:

Not applicable.

6 Pharmacological properties:

6.1 Pharmacodynamic properties:

Pharmaco-therapeutic group: Bacterial and Viral vaccines combined, ATC Code: J07CA11.

Results obtained from a clinical study evaluating the Shan 5 vaccine used as a three dose primary series in the target age group are summarized in table below.

**Seroresponse/ Seroprotection Rates (Percentage of subjects with antibody titers \( \geq \) the pre-defined limits after primary vaccination with Shan 5)**

<table>
<thead>
<tr>
<th>Antibody (cut-off)</th>
<th>Shan 5 (Three doses at 6-8, 10-12 &amp; 14-16 weeks) N=819</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-wcP (( \geq ) 11 NTU)</td>
<td>70.1%</td>
</tr>
<tr>
<td>Anti-PRP (( \geq ) 0.15 mcg/mL)</td>
<td>99.5%</td>
</tr>
<tr>
<td>Anti-HBsAg (( \geq ) 10 mIU/mL)</td>
<td>97.8%</td>
</tr>
<tr>
<td>Anti-Diphtheria (( \geq ) 0.01 IU/mL)</td>
<td>100.0%</td>
</tr>
<tr>
<td>Anti-Tetanus (( \geq ) 0.01 IU/mL)</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

N= Number of subjects with available data
6.2 Pharmacokinetic properties:
Evaluation of pharmacokinetic properties is not required for vaccines.

6.3 Pre-clinical Safety data:
The nonclinical safety evaluation of Shan 5 was assessed in both acute and repeat dose
toxicity studies. The toxicity of Shan 5 was assessed in two acute studies in Wistar rats
and Swiss albino mice, two repeated dose studies in Wistar rat and New Zealand rabbit
and a local skin sensitization study in CBA/J Strain mice.
The events observed in the animals were either considered as a normal expected response
or the expected local response to aluminum adjuvanted vaccines. Shan 5 administration
was associated with no increased risk of adverse events as compared to a licensed
pentavalent vaccine used as a comparator in the toxicology studies conducted.

6.4 Clinical Experience:
In a Phase III study designed to evaluate immune lot consistency and immune non
inferiority of Shan 5 as compared to a licensed pentavalent vaccine, conducted at eleven
centers across India, 1100 subjects (15 toddlers and 1085 infants) were vaccinated. The
study demonstrated seroprotection rates for Hib (99.5%), Hepatitis B (97.8%), Diphtheria
(100%), Tetanus (100%) and seroresponse rate of 70.1% for whole cell Pertussis
component of Shan 5 vaccine as evaluated after a three dose primary series administered
at 6-8, 10-12 and 14-16 weeks of age. The seroprotection/seroresponse rates were
statistically non inferior to the licensed comparator pentavalent vaccine for all five
antigens. The solicited and unsolicited local and systemic adverse events were comparable
between Shan 5 and comparator groups and Shan 5 was considered as safe and well
tolerated in the study age group.

7 Pharmaceutical Particulars:

7.1 List of Excipients:

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Name of the Excipients</th>
<th>Quantity per single dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Thiomersal I.P</td>
<td>0.05 mg</td>
</tr>
<tr>
<td>2.</td>
<td>Aluminium Phosphate equivalent to Al+++</td>
<td>0.625 mg</td>
</tr>
<tr>
<td>3.</td>
<td>Sodium Chloride I.P</td>
<td>4.5 mg</td>
</tr>
<tr>
<td>4.</td>
<td>Water for Injection I.P</td>
<td>q.s. to 0.5 mL</td>
</tr>
</tbody>
</table>

q.s. – Quantity sufficient

7.2 Incompatibilities:
In the absence of compatibility studies, this vaccine must not be mixed with other
medicinal product.
7.3 Shelf-Life:

24 months.

7.4 Special precautions for storage:

Shan 5 should be stored at + 2°C to + 8°C (35.6°F to 46.4°F). Not to be frozen. Discard vaccine if frozen.

7.5 Nature and content of container:

Shan 5 is supplied in Type I glass vials containing 0.5 mL as a single dose and 5.0 mL as a 10 dose.

7.6 Instruction for use and handling:

Shan 5 is presented as a suspension. Upon storage, a white deposit may be observed at the bottom of the vial. The vaccine vial should be shaken adequately in order to obtain a homogeneous turbid white suspension. The vial should be visually inspected for any foreign particulate matter. Physical aspects like cap and the seal should be inspected for integrity of container closure system. In the event of either of the above being observed, discard the vaccine.

When using a multi dose vial, each dose should be taken with a sterile needle and syringe. Each dose of vaccine should be withdrawn under strict aseptic conditions and precautions to avoid contamination of the contents.

8 Marketing authorization holder:

SHANTHA BIOTECHNICS PRIVATE LIMITED (A SANOFI COMPANY)
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Fax Nos. +91(40) 23234133/23234103
E-mail: Info.Shantha@sanofi.com
Website: www.shanthabiotech.com

9 Marketing Authorization Number:

MF-55/2014

10 Date of first authorization/Renewal of Authorization

Date of first issue : 07 March 2014

References: Data on File. Shantha Biotechnics Limited.

02/2015