SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis-B (rDNA) and Haemophilus type b Conjugate Vaccine (Adsorbed) I.P.

Injectable, Suspension for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Diphtheria, Tetanus, Pertussis, Hepatitis-B and Haemophilus Influenzae type b conjugate vaccine adsorbed is a homogenous liquid containing purified diphtheria and tetanus toxoids, inactivated whooping cough (pertussis) organisms, highly purified, non-infectious particles of Hepatitis-B surface antigen (HBsAg) and Hib component as a bacterial subunit vaccine containing highly purified, non-infectious Haemophilus Influenzae type b (Hib) capsular polysaccharide chemically conjugated to a protein (Tetanus toxoid). Surface antigen of the Hepatitis B virus (HBV) is obtained by culturing genetically engineered *Hansenula polymorpha* yeast cells having the surface antigen gene of the Hepatitis B virus. The Hepatitis B surface antigen (HBsAg) expressed in the cells of *Hansenula polymorpha* is purified through several chemical steps using recombinant DNA procedures. Thiomersal is added as preservative. The vaccine meets the requirements of WHO when tested by the methods outlined in WHO, TRS (1990), 800 and 786 (1989).

The Hib polysachharide is prepared from capsular polysaccharide of H. Influenzae type B strain and after activation is coupled to Tetanus Toxoid.

Each dose of 0.5 ml contains:

Diphtheria Toxoid	≤ 25 Lf (≥ 30 IU)
Tetanus Toxoid	≥ 2.5 Lf (≥ 40 IU)
B. pertussis (whole cell)	≤ 16 OU (≥ 4 IU)
HBsAg (rDNA)	≥ 10 mcg
Purified Capsular Polysaccharide (PRP) conjugated to Tetanus Toxoid (carrier protein)	10 mcg
Adsorbed on aluminium phosphate, Al^{+++}	≤ 1.25 mg
Preservative: Thiomersal	0.005%

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Diphtheria, Tetanus, Pertussis, Hepatitis-B and Haemophilus Influenzae type be conjugate vaccine adsorbed is a homogenous liquid containing purified diphtheria and tetanus toxoids, inactivated whooping cough (pertussis) organisms, highly purified, non-infectious particles of Hepatitis-B surface antigen (HBsAg) and Hib component.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DTP-HB-Hib vaccine adsorbed is indicated for the active immunization of infants, at or above the age of 6 weeks against Diphtheria, tetanus, whooping cough, Hepatitis B and Haemophilus Influenzae type b infections.

In young children, the EPI recommends as many antigens as possible to be administered at a single visit.

DTP-HB-Hib vaccine should not be used for the birth dose.

4.2 Posology and method of administration

Posology:

For active immunization of infants and preschool children, it is recommended that three intramuscular injection of 0.5ml be administered with an interval of four weeks between doses starting at six weeks of age. In countries, where peri-natal transmission of HB is common, the first dose of HB should be given as soon as possible after birth. In this case, the combination vaccine can be used to complete the primary series from 6 weeks of age.

A booster dose of DTwP and Hib can be given at the age of 15-18 months.

A reinforcing injection of DTwP should be administered at 5 years of age (i.e. at the time of school entry). IAP (Indian Academy of Pediatrics) recommends that wherever combination vaccines are available they can be substituted for monovalent formulations in the national immunisation schedule wherever indicated.

Administration:

The user must, using a sterile 1 ml or 0.5 ml syringe with a sterile needle extract one dose (0.5 ml) from the single/ multidose vial, on which the outer surface of the stopper has been disinfected with a disinfectant. For each new dose extract 0.5 ml using a new sterile syringe fitted with a sterile needle.

Do not inject subcutaneously or intravenously. The vaccine should be administered by intramuscular injection. The anterolateral aspect of the thigh is the preferred injection site for infants and deltoid for children. Another injection if co-administered with DTP-HB-HIB vaccine should be made at a different site. Only sterile needles and syringes should be used for each injection.

Once opened, multi-dose vials should be kept between 2°C to 8°C. Multi-dose vials of DTP-HB-HIB 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 6 hours, 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 withdraw all doses;

- The vaccine vial monitor (VVM), if attached, has not reached the discard point.

4.3 Contraindications

Hypersensitivity to any component of the vaccine. It is a contraindication to use this or any other related vaccine after an immediate anaphylactic reaction associated with a previous dose. It is a contraindication to administer the vaccine in the presence of any evolving neurological condition. Encephalopathy after a previous dose is a contraindication to further use. Immunization should be deferred during the cause of an acute illness. Vaccination of infants and children with severe, febrile illness should generally be deferred until recovery. However, the presence of minor illnesses such as mild upper respiratory infections with or without low-grade fever is not contraindications to further use. Elective immunization procedures should be deferred during an outbreak of poliomyelitis.

4.4 Special warnings and precautions for use

Warnings:

Due to the long incubation period of Hepatitis B (up to 6 months or more), cases where prior exposure to Hepatitis B virus has taken place, vaccination may not be effective. If any of the following events occur in temporal relation to receipt of PENTAVAC SD/MD, the decision to give subsequent doses of vaccine containing the pertussis component should be carefully considered. Temperature 40.5°C (105°F) or more within 48 hours of a dose unexplained by another cause. Collapse or shock-like state (hypotonic-hypo responsive episode) within 48 hours. Persistent, inconsolable crying lasting 3 hours or more occurring within 48 hours. Convulsions with or without fever occurring within three days. There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks, particularly since these events are not associated with permanent sequelae. PENTAVAC SD/MD should not be given to children with any coagulation disorder, including thrombocytopenia that would contraindicate intramuscular injection unless the potential benefit clearly outweighs the risk of administration. Infants and children with a history of convulsions in first-degree family members (i.e. siblings and parents) when administered DTP containing vaccine have an increased risk for neurologic events and permanent neurologic damage when compared with infants without such history. Infants and children with recognized possible or potential underlying neurologic conditions seem to be at enhanced risk for the appearance of manifestation of the underlying neurologic disorder within two or three days following vaccination. The administration of PENTAVAC SD/MD to children with proven or suspected underlying neurologic disorders that are not actively evolving must be decided on an individual basis.

Precautions:

Prior to an injection of any vaccine, all known precautions should be taken to prevent adverse reactions. This includes a review of the parent's history with respect to possible sensitivity and any previous adverse reactions to the vaccine or similar vaccines. Previous immunization history, current health status and a current knowledge of the literature concerning the use of the vaccine under consideration. Immunosuppressed children may not respond.

Prior to administration of PENTAVAC SD/MD, health care personnel should inform the guardian of the child the benefits and risks of immunization, and also inquire about the recent health status of the child to be injected. Parents of a child with a family history of seizures should be informed that their child has an increased risk of seizures following administration of any DTP containing vaccine and should be instructed regarding appropriate medical care in the unlikely event of a seizure. Special care should be taken to ensure that the injection does not enter a blood vessel.

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 s/c or i/m. Single dose should not exceed 1 mg (1 ml). For infants and children the recommended dose of adrenaline is 0.01 mg/kg (0.01 ml/kg of 1:1000 injection). Single pediatric dose should not exceed 0.5 mg (0.5 ml). The mainstay in the treatment of severe anaphylaxis is the prompt use of adrenaline, which can be lifesaving.

As with the use of all vaccines, the vaccine should remain under observation for not less than 30 minutes for possibility of occurrence of immediate or early allergic reactions. Efcorlin hydrochloride and antihistaminics should also be available in addition to supportive measures such as oxygen inhalation.

4.5 Interaction with other medicinal products and other forms of interaction
As with other intramuscular injections, use with caution in patients on anticoagulant therapy. Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses) may reduce the immune response to vaccines. Short-term (< 2 weeks) corticosteroid therapy or intra-articular, bursal or tendon injections with corticosteroids should not be immunosuppressive.

4.6 Pregnancy and lactation
Not recommended to be used in pregnant or lactating mothers.

4.7 Effects on the ability to drive and use machines
Not applicable.

4.8 Undesirable effects
Adverse reactions associated with the use of this vaccine include local redness, warmth, oedema, and induration with or without tenderness, as well as urticaria and rash. Systemic reactions such as fever, headache, drowsiness, weakness, fretfulness, nausea, vomiting, diarrhoea and anorexia may occur in a few infants. Some data suggests that febrile reactions are more likely to occur in those who have experienced such responses after prior doses of DTP vaccine. High fever (i.e. temperature of 40.5°C (105°F) and persistent, inconsolable crying lasting 3 hours or more has been reported. These events occur infrequently and appear to be without sequelae. If your child already presented with febrile convulsions, not related to aprevious vaccine injection, in this case it is particularly important that temperature be monitored in the 48 hours following vaccination and that antipyretic treatment be regularly administered to help reduce fever, for 48 hours Occasionally, a nodule may be

palpable at the injection site of adsorbed products for several weeks. Sterile abscesses at the site of injection have been reported (6 to 10 per million doses).

In study conducted on PENTAVAC, the frequency of local and systemic reactions was not higher with subsequent doses and was well within the range of other DTP containing vaccines.

Evidence does not indicate a causal relation between DTP vaccine and SIDS. Studies showing a temporal relation between these events are consistent with the expected occurrence of SIDS over the age range in which DTP immunization typically occurs. No association has been shown for hospitalizations due to infectious diseases and receipt of DTP.

Nervous system
The following neurologic illnesses have been reported as temporally associated with vaccine containing tetanus toxoid; neurological complications including cochlear lesion, brachial plexus neuropathies, paralysis of the radial nerve, paralysis of the recurrent nerve, accommodation paresis, and EEG disturbances with encephalopathy. It has been suggested that there is a causal relation between Guillain-Barre syndrome (GBS) and vaccines containing tetanus toxoid. In the differential diagnosis of polyradiculoneuropathies following administration of a vaccine containing tetanus toxoid should be considered as a possible etiology. Short-lived convulsions (usually febrile), or collapse (hypotonic hyporesponsive episode) occur infrequently and appear to be without sequelae.

More severe neurologic events, such as a prolonged convulsion or encephalopathy, although rare, have been reported in temporal association with DTP administration. An analysis of these data failed to show any cause and effect association.

Cardiovascular system
An infant who developed myocarditis several hours after immunization has been reported.

Respiratory system
Respiratory difficulties including apnea have been observed.

Local
Rash and allergic reactions have been observed.

4.9 Overdose
No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines,

Combined vaccines, ATC code J07CA11.

Immunological Data:
Various clinical trials performed to assess Immunogenicity and reactogenicity of the vaccine and proved that the vaccine is efficacious.

5.2 Pharmacokinetic properties
Not applicable.

5.3 Preclinical safety data
No mortality or abnormal clinical signs were observed in animals treated with test vaccine during the observational period. The study vaccine did not induce any adverse effect on the rate of body weight gain and food intake. No significant finding was seen in hematology, biochemical parameters and in organ weights.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients
Aluminium Phosphate (Prepared from Aluminium chloride + Tri-sodium phosphate)
Thiomersal
Sodium chloride
Sodium Acetate
Water for Injection

6.2 Incompatibilities
This product must not be mixed with other medicinal products.

6.3 Shelf-life
Do not exceed the expiry date stated on the external packing.

6.4 Special precautions for storage
The components of the combination vaccine must be stored and transported between 2ºC to 8ºC. The DTP HepB component must not be frozen.

6.5 Nature and contents of container

Single dose presentation	:	1 dose pre-filled syringe of 0.5 ml 1 dose ampoule of 0.5 ml 1 dose vial of 0.5 ml
Multi-dose presentation	:	2 dose vial of 1 ml 5 dose vial of 2.5 ml 10 dose vial of 5 ml

6.6 Special precautions for disposal
Any unused product or waste material should be disposed of in accordance with local requirements.

SUMMARY OF PRODUCT CHARACTERISTICS

7. MARKETING AUTHORISATION HOLDER / PREQUALIFICATION HOLDER

Name: Serum Institute of India Ltd.
Address: 212/2, Hadapsar, Pune - 411 028, Maharashtra, INDIA.
Telephone No: 91-20-26993900, 91-20-26602378
Fax No: 91-20-26993945
E-mail: ssj@seruminstitute.com

8. MARKETING AUTHORISATION NUMBER(S)

Permission No. – **MF-167/09** (Form 46).

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorization – 12.02.2009
Renewal of authorization – 01.01.2012

01/2014