1. NAME OF THE MEDICINAL PRODUCT

Diphtheria, Tetanus, Pertussis (Whole Cell) and Hepatitis B (rDNA) Vaccine (Adsorbed) I.P.

Injectable, Suspension for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 0.5 ml contains:

Diphtheria Toxoid	≤ 25 Lf (≥ 30 IU)
Tetanus Toxoid	≥ 5 Lf (≥ 40 IU)
B. pertussis (whole cell)	≤ 16 OU (≥ 4 IU)
HBsAg (rDNA)	≥ 10 mcg
Adsorbed on aluminium phosphate, Al^{+++}	≤ 1.25 mg
Preservative: Thiomersal	0.005%

For a full list of excipients, see section 6.1.

DTP-HB vaccine does not prevent Hepatitis caused by other agents different from HBV (as virus A, C and E) but it is considered effective in preventing Hepatitis caused by the delta agent.

3. PHARMACEUTICAL FORM

Suspension for injection.

Sterile, opaque, grayish - white uniform suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Diphtheria, Tetanus, Pertussis (Whole Cell) and Hepatitis B (rDNA) Vaccine (DTP-HB) Vaccine (Adsorbed) is indicated for the active immunization of infants, at or above the age of 6 weeks of birth and of children through 6 years of age against diphtheria, tetanus, whooping cough and Hepatitis B.

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

The combined vaccine can be given safely and effectively at the same time as BCG, Measles and Polio vaccines (OPV and IPV), Haemophilus influenzae-B, Yellow Fever vaccines and Vitamin A supplementation.

4.2 Posology and method of administration

Posology:

For active immunization of infants and preschool children, it is recommended that three intramuscular injection of 0.5 ml be administered with an interval of four weeks between doses. Although the customary age of primary immunization is two months but is now recommended to be given at 6 weeks of age. If for any reason it is delayed, the same schedule may be used up to the sixth birth day.

Specifically, IAP recommends DTP to be given at 6, 10 and 14 weeks. A booster of DTP can be given at the age of 1 ½ years and a reinforcing injection of the 0.5 ml intramuscularly of the combination should be administered at 5 years of age (i.e. at the time of school entry).

Administration:

Do not inject subcutaneously or intravenously.

The vaccine vial should be well shaken to get an opaque suspension. 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 vaccine should be administered at a different site. Only sterile needles and syringes should be used for each injection.

How to use SII DTP-Hep B vaccine and SII Hib vaccine as Pentavalent vaccine.

SII DTP-HepB to be used to reconstitute SII Hib vaccine for simultaneous administration via single injection. SII Hib vaccine must be reconstituted by adding the entire contents of SII DTP-HepB ampoules or 0.5 ml of SII DTP-HepB from a multidose vial of SII DTPHepB. After the addition of SII DTP-HepB to Hib pellet, the mixture should be well shaken until the Hib pellet is completely dissolved in the SII DTP-HepB suspension. After reconstitution the combined vaccine should be injected promptly. Inject 0.5 ml suspension by intramuscular injection.

The vaccine should be visually inspected for any foreign particulate matter and / or variation of physical aspect prior to administration. In event of either being observed, discard the vaccine.

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 course 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 (upto 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 DTP, the decision to give subsequent doses of vaccine containing the pertussis component should be carefully considered. 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.

- Temperature 40.5°C (105°F) or more within 48 hours of a dose unexplained by another cause.
- Collapse or shock-like state (hypotonic-hyporesponsive 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.

Persons who experience Arthus-type hypersensitivity reactions or a temperature of 39.4°C (> 103° F) following a prior dose of tetanus toxoid usually have high serum tetanus antitoxin levels and should not be given even emergency doses of Td vaccine more frequently than every 10 years even if they have a wound that is neither clean not minor.

DTP-HB vaccine 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.

Recent studies suggest that infants and children with a history of convulsions in first-degree family members (i.e. siblings and parents) have a 3:2 fold increased risk for neurologic events compared DTP vaccine and permanent neurologic damage 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 DTP-HB vaccine 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 patients may not respond.

Prior to administration of DTP-HB vaccine, health care personnel should inform the patient or guardian of the patient the benefits and risks of immunization, and also inquire about the recent health status of the patient 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 DTP-HB vaccine administration 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. WHO does not recommend mixing different vaccines in one syringe before injection.

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 (0.1-0.5ml of 1:1000 injection) given s/c or i/m. Single dose should not exceed 1 mg (1ml). For infants and children the recommended dose of adrenaline is 0.01mg/kg (0.01ml/kg of 1:1000 injection). Single pediatric dose should not exceed 0.5mg (0.5ml). 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 vaccinee should remain under observation for not less than 30 minutes for possibility of occurrence of immediate or early allergic reactions. Hydrocortisone 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 immuno-suppressive.

4.6 Pregnancy and lactation

No clinical data on use during pregnancies are available with this vaccine, as this vaccine is intended for use in Pediatric population (< 6 years of age) only.

4.7 Effects on the ability to drive and use machines

No data available on effects on the ability to drive and use machines for this vaccine, as this vaccine is intended for use in Pediatric population only.

4.8 Undesirable effects

Mild, local reactions are common. Some temporary swelling, tenderness and redness at the site of injection together with fever occur in large proportion of cases. Occasionally severe reactions of high fever, irritability and screaming develop within 24 hours of administration. Hypotonic-hypo responsive episodes have been reported rarely. Administration of paracetamol at the time of and 4-8 hours after immunization decreases the subsequent incidents of febrile reactions. The national childhood encephalopathy study in the United Kingdom showed a small increases risk of acute encephalopathy (primary seizures) following DTP immunization. However subsequent detailed reviews of all available studies by a number of groups, including the United States Institute of Medicine, the Advisory Committee of Immunization Practices, and the pediatric association of Australia, Canada the United Kingdom, and the United States concluded that the data did not demonstrate the causal relationship between DTP and chronic nervous system dysfunction in children. Thus there is no scientific evidence that hypotonic-hypo responsive episode and febrile convulsions have any permanent consequences for the children.

Hepatitis B vaccine is very well tolerated. In placebo controlled studies, with exception of local pain, reported events such as myalgia, and transient fever have not been more frequent than in a placebo group. Reports of severe anaphylactic reactions are very rare. Available data do not indicate a casual association between hepatitis B vaccination and Guillain Barre Syndrome or demyelinating disorders including multiple sclerosis, nor is there any epidemiological data to support a causal association between hepatitis B vaccination and chronic fatigue syndrome, arthritis autoimmune disorders, asthma, sudden infant death syndrome, or diabetes.

IMMUNE DEFICIENCY

Individuals infected with the human immuno-deficiency virus (HIV), both asymptomatic and symptomatic, should be immunized with combined vaccine according to standard schedules.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines,

Diphtheria-Hepatitis B-Pertussis-Tetanus, ATC code J07CA05.

Immunological Data:

Various clinical trials performed to assess Immunogenicity and reactogenicity of the vaccine proved that the vaccine is immunogenic.

In a trial in New Delhi, India, the DTP-HB vaccine was administered in 75 healthy infants in a dose of 0.5 ml at 6, 10 and 14 weeks. Following vaccination, the seropositivity for pertussis was 97.33%, and seroprotection was 100% for diphtheria, tetanus and Hepatitis B.

In a trial in Mumbai, India, the DTP-HB vaccine was administered in 75 healthy infants in a dose of 0.5 ml at 6, 10 and 14 weeks. Following vaccination, the seroprotection for diphtheria was 98.66%, and 100% for tetanus and Hepatitis B, and for pertussis, seropositivity was 94.6%.

In a trial in Pune, India, the DTP-HB vaccine was administered in 143 healthy infants in a dose of 0.5 ml at 6, 10 and 14 weeks. Following vaccination, the seroprotection for diphtheria was 99.19%, tetanus was 98.3%, and for Hepatitis B, it was 100%, and for pertussis, seropositivity was 88.62%.

5.2 Pharmacokinetic properties

Pharmacokinetic studies are not required for vaccines.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional animal studies consisting of acute and repeated dose toxicity.

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

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

6.3 Shelf-life

24 months from the date of manufacturing.

6.4 Special precautions for storage

The vaccine should be stored in a dry, dark place at a temperature between 2°C to 8°C. Transportation should also be at 2°C to 8°C. DO NOT FREEZE.

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 ampoule of 1 ml
		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.

7. MARKETING AUTHORISATION HOLDER / PREQUALIFICATION HOLDER

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Address: 212/2, Hadapsar, Pune - 411 028, Maharashtra, INDIA.

Telephone No: +91-20-26993900

Fax No: +91-20-26993921

E-mail: contact@seruminstitute.com

8. MARKETING AUTHORISATION NUMBER(S)

Permission No. - MF-2090/05 (Form 46).

Manufacturing License No. 10 in Form 28-D

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorization: 28.02.2005

Date: 31 December 2022