SUMMARY OF THE PRODUCT CHARACTERISTICS

1.0 NAME OF THE MEDICINAL PRODUCT:

Diphtheria, Tetanus, Pertussis, Hepatitis-B and Haemophilus influenzae type b Conjugate Vaccine Adsorbed

2.0 QUALITATIVE AND QUANTITATIVE COMPOSITION:

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 Hib Polysaccharide (PRP) Conjugated to Tetanus Toxoid (carrier protein)	10 mcg
Adsorbed on Aluminium Phosphate, Al^{+++}	≤ 1.25 mg
Preservative: Thiomersal	0.005 %

3.0 PHARMACEUTICAL FORM :

Suspension for injection
Whitish turbid liquid

4.0 CLINICAL PARTICULARS:

4.1 Indications:

Diphtheria, Tetanus, Pertussis, Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Adsorbed is indicated for the active immunization of infants, at or above the age of 6 weeks against Diphtheria, tetanus, pertussis, Hepatitis B and *Haemophilus Influenzae* type b.

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

Diphtheria, Tetanus, Pertussis, Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Adsorbed should NOT be used for the birth dose.

In countries where Pertussis is of particular danger to young infants, the combination vaccine should be started as soon as possible with the first dose given as early as 6 weeks, and two subsequent doses given at 4-week intervals.

The Diphtheria, Tetanus, Pertussis, Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Adsorbed can be given safely and effectively at the same time as BCG, measles, polio (OPV or IPV), and yellow fever vaccines and vitamin A supplementation. If Diphtheria, Tetanus, Pertussis, Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Adsorbed is given at the same time as other vaccines, it should be administered at a separate site. It should not be mixed in the vial or syringe with any other vaccine unless it is licensed for use as a combined product.

SUMMARY OF THE PRODUCT CHARACTERISTICS (SPC)

4.2 Posology and method of administration:

Dosage:

For active immunization of infants and pre-school 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 for first dose of primary immunization is two months but is now recommended to be given at 6 weeks of age. A booster dose of DTwP and *Haemophilus influenzae* type b Conjugate Vaccine can be given at the age of 15-18 months.

A reinforcing injection of DTwP vaccine 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:

Do not inject subcutaneously or intravenously.

The liquid vaccine vial should be shaken before use to homogenize the suspension. The vaccine should be injected intramuscularly. The anterolateral aspect of the upper thigh is the preferred site of injection, or into the deltoid muscles of older children or adults. An injection into a child's buttocks may cause injury to the sciatic nerve and is not recommended. It must not be injected into the skin as this may give rise to local reaction. One paediatric dose is 0.5 ml. A sterile syringe and sterile needle must be used for the injection. The vaccine should be administered by intramuscular injection.

Another injection if coadministered with Diphtheria, Tetanus, Pertussis, Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Adsorbed 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 +2ºC and +8ºC. Multi-dose vials of Diphtheria, Tetanus, Pertussis, Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Adsorbed from which one or more doses of vaccine have been removed during an immunisation session may be used in subsequent immunisation sessions for upto a maximum of 28 days, provided that all of the following conditions are met (as described in the WHO policy statement: Handling of multi dose vaccine vials after opening, WHO/IVB/14.07):

- The vaccine is currently prequalified by WHO;
- The vaccine is approved for use for up to 28 days after opening the vial, as determined by WHO;
- The expiry date of the vaccine has not passed;
- The vaccine vial has been, and will continue to be, stored at WHO - or manufacturer recommended temperatures; furthermore, the vaccine vial monitor, if one is attached, is visible on the vaccine label and is not past its discard point, and the vaccine has not been damaged by freezing.

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 Contraindication:

Known hypersensitivity to any component of the vaccine, or a severe reaction to a previous dose of the combination vaccine or any of its constituents is an absolute contraindication to subsequent doses of the combination vaccine or the specific vaccine known to have provoked an adverse reaction. There are few contraindications to the first dose of DTP - fits or abnormal cerebral signs in the newborn period or other serious neurological abnormality are contraindications to the pertussis component. In this case, the vaccines should not be given as a combination vaccine but DT should be given instead of DTP and Hep B and Hib vaccines given separately. The vaccine will not harm individuals currently or previously infected with the hepatitis B virus.

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 40.5ºC (105ºF) 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 39.4ºC (>103ºF) following a prior dose of tetanus toxoid usually have high serum tetanus antitoxin levels and should not be given even emergency doses of Td more frequently than every 10 years even if they have a wound that is neither clean not minor.

DTP 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 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 DTPHep B Hib, 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 DTP 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.

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 paediatric 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 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

Drug Interactions:

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 Fertility, Pregnancy and lactation:

Not recommended to be used in pregnant or lactating mothers.

4.7 Effects on 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, edema, and induration with or without tenderness, as well as urticaria and rash. Systemic reactions such as fever, headache, nausea and weakness may appear in a few subjects. Some data suggests that febrile reactions are more likely to occur in those who have experienced such responses after prior doses.

The type and rate of severe adverse reactions do not differ significantly from the DTP, HepB and Hib vaccine reactions described separately.

For DTP, mild local or systemic reactions are common. Some temporary swelling, tenderness and redness at the site of injection together with fever occur in a large proportion of cases. Occasionally severe reactions of high fever, irritability and screaming develop within 24 hours of administration. Hypotonic-hyporesponsive episodes have been reported. Febrile convulsions have been reported at a rate of one per 12500 doses administered. Administration of acetaminophen at the time and 4-8 hours after immunization decreases the subsequent incidence of febrile reactions. The national childhood encephalopathy study in the United Kingdom showed a small increased risk of acute encephalopathy (primarily 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 on Immunization Practices, and the paediatric associations of Australia, Canada, the United Kingdom and the United States, concluded that the data did not demonstrate a causal relationship between DTP and chronic nervous system dysfunction in children. Thus there is no scientific evidence that these reactions have any permanent consequences for the children.

Hepatitis B vaccine is very well tolerated. In placebo-controlled studies, with the exception of local pain, reported events such as myalgia and transient fever have not been more frequent than in the placebo group. Reports of severe anaphylactic reactions are very rare. Available data do not indicate a causal association between hepatitis B vaccine and Guillain Barré 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.

Hib vaccine is very well tolerated. Localized reactions may occur within 24 hours of vaccination, when recipients may experience pain and tenderness at the injection site. These reactions are generally mild and transient. In most cases, they spontaneously resolve within two to three days and further medical attention is not required. Mild systemic reactions, including fever, rarely occur following administration of Hib vaccines. More serious reactions are very rare; a causal relationship between more serious reactions and the vaccine has not been established.

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.

5.0 PHARMACOLOGICAL PROPERTIES:

Category: Bacterial and viral vaccines, combined
ATC code: J07CA11

5.1 Pharmacodynamic properties:

Post-vaccination percentage sero-protection

For Diphtheria, Tetanus, Hepatitis B and Haemophilus influenzae type 'b', there was 100% seroprotection. For Pertussis, percentage vaccine response was 95.3 %.

Post-vaccination Geometric Mean Titres

Post-vaccination Geometric Mean Titres were 1.27 IU/ml, 3.15 IU/ml, 46.11 U/ml, 433.0 mIU/ml and 6.72 ug/ml for anti Diphtheria, anti-Tetanus, anti-Pertussis, anti Hepatitis B and anti PRP IgG antibodies.

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.

6.0 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 packaging.

6.4 Special precautions for storage:

The vaccine should be stored at a temperature between 2-8°C. Transportation should also be at 2-8°C. DO NOT FREEZE.

6.5 Nature and contents of container:

1 dose vial : 2 ml clear tubular type I glass vial (Ht: 30mm, Diameter: 16.5mm); sealed with 13mm rubber stopper and 13mm violet flip-off seal.

10 dose vial : 5 ml clear tubular type I glass vial (Ht: 52mm, Body diameter: 16.5mm); sealed with 13mm rubber stopper and 13mm violet flip-off seal.

6.6 Special precautions for disposal:

Any unused product or waste material should be disposed of in accordance with local requirements.

7.0 MARKETING AUTHORISATION HOLDER:

SERUM INSTITUTE OF INDIA PVT. LTD
REGD OFFICE AND LABORATORIES
212/2, HADAPSAR, PUNE-411028.
INDIA.
TELEPHONE: ++ 91-20-26993900 / 04
FAX: ++ 91-20-26993924 / 26993921
SITE WEB: www.seruminstitute.com
E-MAIL: serumexports@seruminstitute.com

8.0 MARKETING AUTHORIZATION NUMBER(S):

04501/6413/REN/2018

9.0 DATE OF FIRST AUTHORIZATION/ RENEWAL OF THE AUTHORIZATION:

LAST RENEWAL DATE : May 24, 2019

10. DATE OF REVISION OF THE TEXT:

May 24, 2019