SUMMARY PRODUCT CHARECTERISTICS

Diptheria,Tetaus,Pertiuss Hepatitis and Haemophilus influenza type b Conjugate Vaccine Adsorbed

DESCRIPTION	Diphtheria,Tetanus,Pertussis Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Absorbed as supplied by Serum Institute of India Ltd., is a homogenous liquid containing purified diphtheria and tetanus toxoids, inactivated whopping cough (pertussis) organisms, highly purified, non-infectious particles of Hepatitis B 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 Toxoids). Surface antigen of the Hepatitis B virus (HBV) is obtained by culturing surface antigen (HBsAg) expressed in the cells of Hansenula ploymorpha is purified through several chemical steps using recombinant DNA procedures. Thiomersal is added as preservative. The Hib polysaccharide is prepared from capsular polysaccharide of *H. influenzae* type b stain and after activation is coupled to Tetanus Toxoids. The vaccine meets the requriments of W.H.O and B.P when tested by the methods outlined in W.H.O., TRS. 980 (2014), 978 (2013), 897 (2000) and B.P.
POTENCY	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 (≥4.0 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% *The lower fiducial limit (P=0.95) of the estimated potency is not less than 2.0 IU. Diphtheria,Tetanus,Pertussis Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Absorbed does not prevent Hepatitis caused by the agents different from HBV (as virus A, C and E) but it is considered effective in preventing Hepatitis caused by delta agent. HIB vaccine does not protect against disease due to other types of *H.influenzae* nor against meningitis caused by other organisms
THERAPEUTIC INDICATIONS	Diphtheria,Tetanus,Pertussis Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Absorbed is indicated for the active immunization of infants, at or above the age of 6 weeks against Diphtheria, tetanus, pertussis 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 Absorbed should not be used for 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. Diphtheria,Tetanus,Pertussis Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Absorbed 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 Absorbed 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.
DOSAGE & METHOD OF ADMINISTRATION	For active immunization of the infants and pre-school children, it is recommended that the three intramuscular injection of 0.5 ml be administered with an interval of four weeks between dosses. Although the customary age for the first dose of primary immunization is

	two months but is now recommended to be given at 6 weeks of age. A booster dose if DTwp and *Haemophilus influenzae* type b Conjugate Vaccine can be at the age of 15-18 months. A reinforcing 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 immunization schedule wherever indicated. 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 upper thigh is 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 pediatricdose 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 coadministered with Diphtheria,Tetanus,Pertussis Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Absorbed should be made at different site. Only sterile syringes should be used for each injection. Once opened, multi-dose vial should be kepet between +2 °C and +8 °C. Multi-dose vials of Diphtheria,Tetanus,Pertussis Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Absorbed from one or more doses of the vaccine have been removed during immunization session may be used in subsequent immunization sessions for upto a maximum of 4 weeks provided that all of the following conditions are met 1. The expiry date has not passed. 2. The vaccines are stored under appropriate cold chain conditions; 3. The vaccine vial septum has not been submerged in water; 4. Aseptic technique has been used to withdraw all doses; 5. The vaccine vial monitor (VVM), if attached, has not reached the discard point. The vaccine should be visually inspected for any foreign particulate matter and /or variations of physical aspect prior to the administration. In event of either being observed discard the vaccine.
CONTRAINDICATONS	Known hypersensitivity to any component of the vaccine, or severe reaction to a pervious dose of the combination vaccine or any of its constituents is an absolute 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 hepatitis B virus.
SPECIAL WARNINGS & PRECAUTION FOR USE	Due to the long incubation period of Hepatitis B (upto 6 months or more), case where prior exposure to Hepatitis B virus has taken place, vaccines may not be effective. If any of the following events occur in temporal relation to the receipt of DTP, the decision to give subsequent doses of vaccine containing the pertussis component should be carefully considered. There may be circumstances such high incidence of pertussis, when the potential benefits outweigh possible risks, particularly since these events are not associated with permanent sequelae. 1. Temperature 40.5°C (105°F) or more within 48 hours of a dose unexplained by another cause. 2. Collapse or shock- like state (hypotonic-hyporesponsive episode) within 48 hours. 3. Persistent, inconsolable crying lasting 3 hours or more occurring within 48 hours. 4. Convulsions with or without fever occurring within three days.

	Persons who experience Arthus-type hypersensitivity reactions or a temperature of 39°C (> 103°F) following a prior dose of tetanus toxoid usually have high serum tetanus antitoxin levels and should and should not be given emergency doses of Td more frequently than 10 years eve 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 risks of administration. Recent studies suggest that infants and children with a history of convulsions in the first-degree family members (i.e. siblings and parents) have 3:2 fold increase 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 DTO to children with proven or suspected underlying neurologic disorders that are not actively evolving must be decided on an individual basis. Prior to an injection of any vaccine, all know 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 immunizations history, current health status and current knowledge of the literature concerning the use of 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 ricks of the immunization, and also inquire about the recent health status of the child to be injected. Parents of a child with 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 ACUTE ANAPHYLACTIC REACTION OCCUR DUE TO ANY COMPONET 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 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.
INTERACTION WITH OTHER MEDICAL PRODUCTS & OTHER FORM 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) corticosteroids therapy or intra-articular, bursal, or tendon injections with corticosteroids should not be immunosuppressive. **Adverse Reactions**

	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 subject. Some data suggests that febrile reaction are more likely to occur in t 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 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 United Kingdom showed a small increased risk of acute encephalopathy (primary seizures) following DTP immunization. However subsequent detailed reviews of all available studies by a number of groups, including United States institute of Medicine, the Advisory Committee on Immunization Practices, and the pediatric 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 not been more frequent than in placebo group. Reports of severe anaphylactic reactions are very rare. Available data do not indicate a causal association between hepatitis B vaccine and Guillain Barre syndrome, or demyelinating disorders including multiple sclerosis, nor is there any epidemiological data to support a casual association between hepatitis b vaccination and chronic fatigue syndrome, arthritics, autoimmune disorders, asthma, sudden infant death syndrome, or diabetes. Hip vaccine is very well tolerated. Localized reactions may occur within 24 hours hour 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 2 to 3 days and further medical attention not required. Mild systemic reactions, including fever, rarely occur following administration of Hib vaccination. More severe reactions are very rare; a causal relationship between more serious reactions and the vaccination has not been established.
UNDESIRABLE EFFECTS	The type and rate of severe adverse reactions do not differ significantly from the measles and rubella vaccine reactions described separately. The measles vaccine may cause within 24 hours of vaccination mild pain and tenderness at the injection site. In most cases, they spontaneously resolve within two to three days without further medical attention. A mild fever can occur in 5-15% of vaccinees 7 to 12 days after vaccination and last for 1-2 days. Rash occurs in approximately 2% of recipients, usually starting 7-10 days after vaccination and lasting 2 days. The mild side effects occur less frequently after the second dose of a measles-containing vaccine and tend to occur only in person not protected by the first dose. Encephalitis has been reported following measles vaccination at a frequency of approximately one case per million doses administered although a causal link is not proven. The rubella component may commonly result in joint symptoms manifested as arthralgias (25%) and arthritis (10%) among adolescent and adult females that usually last from a few days to 2 weeks. However, such adverse reactions are very rare in children and in men receiving MR vaccine (0%-3%). Symptoms typically begin 1-3 weeks after vaccination and

	last 1 day to 2 weeks. These transient reactions seem to occur in non-immunes only, for whom the vaccine is important. Low-grade fever and rash, lymphadenopathy, myalgia and paraesthesiae are commonly reported. Thrombocytopenia is rare and has been reported in less than 1 case per 30 000 doses administered. Anaphylactic reactions are also rare. In susceptible individuals the vaccine may very rarely cause allergic reactions like urticaria, pruritis and allergic rash within 24 hours of vaccination. Clinical experience has exceptionally recorded isolated reactions involving the CNS. These more serious reactions have however, not been directly linked to vaccination
STORAGE OF VACCINES	The vaccine should be stored in temperature 2- 8°C. Transportation should also be at 2-8°C. DO NOT FREEZE.
PRESENTATION	1 Dose vial of 0.5 ml 2 Dose vial of 1 ml 10 Dose vial of 5 ml
MARKETING AUTHORIZATON HOLDER	Serum Institute of India Ltd.
PRODUCT REGISTRATION NUMBER	BHU-DRA/B02533 BHU-DRA/B02534 BHU-DRA/B02535 BHU-DRA/B02536 BHU-DRA/B02537