

Registration No.: 2C 5/50 (NG)

Importer / Manufacturer: Masu Co., Ltd (BKK) / Serum Institute of India (India)

## SUMMARY OF PRODUCT CHARACTERISTIC

### 1. NAME OF THE MEDICAL PRODUCT

DIPHTHERIA, TETANUS, PERTUSSIS AND HEPATITIS-B VACCINE ADSORBED

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5 ml contains:

Diphtheria Toxoid	$\leq 25$ Lf ( $\geq 30$ IU)
Tetanus Toxoid	$\geq 5$ Lf ( $\geq 40$ IU)
B.Pertussis (whole cell)	$\leq 16$ OU ( $\geq 4$ PU)
HBsAg (rDNA)	$\geq 10$ mcg
Al <sup>+++</sup>	$\leq 1.25$ mg

### 3. PHARMACEUTICAL FORM

Sterile, opaque suspension

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

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), Hib, Yellow Fever vaccines and Vitamin A supplementation.

#### 4.2 Posology and method of 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 coadministered with DTP-HB 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 and +8°C. Multi-dose vials of DTP from which one or more doses of vaccine have been removed during an 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

- 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;

#### 4.3 Contraindication

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 are 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 more frequently than every 10 years even if they have a wound that is neither clean nor 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 patients may not respond. Prior to administration of DTP, 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 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.

#### *4.5 Interaction with other medical products and 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*

-

#### *4.7 Effects on the ability to drive and use machines*

-

#### *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 frequency of local reactions and fever following DTP vaccination is significantly higher with increasing number of doses of DTP, while other mild to moderate systemic reactions. (e.g. fretfulness, vomiting) are significantly less frequent. If local redness 2.5 cm occurs the likelihood of recurrence after another DTP dose increases significantly. Evidence does not indicate a causal reaction 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.

Deaths due to causes other than SIDS including deaths due to serious infections have occurred in infants following the administration of DTP. No association has been shown for hospitalizations due to infectious diseases and receipt of DTP.

Mild systemic reactions such as fever, drowsiness, fretfulness and anorexia occur quite frequently. Rarely, an anaphylactic reaction (i.e. hives, swelling of the mouth, difficulty in breathing, hypertension or shock and death) have been reported after receiving preparations containing diphtheria, tetanus and / or pertussis antigens.

Arthus-type hypersensitivity reactions characterized by severe local reactions (generally starting 2 to 8 hours after an injection), may follow receipt of tetanus toxoid.

Moderate to severe systemic events, including high fever (i.e. temperature of 40.5°C (105°F) and persistent, inconsolable crying lasting 3 hours or more. These events occur infrequently and appear to be without sequelae.

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).

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*

-

## **5. PHARMACOLOGICAL PROPERTIES**

### *5.1 Pharmacodynamic properties*

-

5.2 *Pharmacokinetic properties*

-

5.3 *Preclinical safety data*

-

**6. PHARMACEUTICAL PARTICULARS**

6.1 *List of excipients*

Each 0.5 ml contains:

Thiomersal  $\leq 0.01\%$

6.2 *Incompatibilities*

-

6.3 *Shelf life*

24 months from date of manufacture.

6.4 *Special precautions for storage*

The vaccine should be stored in a dry, dark place 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*

Glass ampoule

6.6 *Special precautions for disposal and other handling*

-

**7. MARKETING AUTHORISATION HOLDER**

MASU CO., LTD.

**8. MARKETING AUTHORISATION NUMBER (S)**

3/2536

**9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION**

1 June 2007

**10. DATE OF REVISION OF THE TEXT**

22 June 2012