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

DESCRIPTION

Diphtheria, Tetanus, Pertussis, Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Adsorbed as supplied by Serum Institute of India Pvt. Ltd., is a homogeneous 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 Hib polysaccharide is prepared from capsular polysaccharide of *H. Influenzae* type b strain and after activation is coupled to Tetanus Toxoid.

The vaccine meets the requirements 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.

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 Adsorbed 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. HIB vaccine does not protect against disease due to other types of *H.Influenzae* nor against meningitis caused by other organisms.

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.

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 +2°C and +8°C. 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.

CONTRAINDICATIONS

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.

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 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.

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.

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 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 symptomatic and symptomatic, should be immunized with combined vaccine according to standard schedules.

STORAGE

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

SHELF LIFE

Do not exceed the expiry date stated on the external packaging.

PRESENTATION

1 dose vial of 0.5 ml
2 dose vial of 1 ml
10 dose vial of 5 ml

THE VACCINE VIAL MONITOR (Optional)

✓ Inner square lighter than outer circle. **If the expiry date has not passed, USE the vaccine.**

✓ At a later time, inner square still lighter than outer circle. **If the expiry date has not passed, USE the vaccine.**

Discard point:

✗ Inner square matches colour of outer circle. **DO NOT use the vaccine.**

Beyond the discard point:

✗ Inner square darker than outer ring. **DO NOT use the vaccine.**

Vaccine Vial Monitors (VVMs) are on the cap (2 ml vial) / part of the label of Diphtheria, Tetanus, Pertussis, Hepatitis B and Haemophilus influenzae type b Conjugate Vaccine Adsorbed supplied through Serum Institute of India Pvt. Ltd. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.

Manufactured by:
SERUM INSTITUTE OF INDIA PVT. LTD.
212/2, Hadapsar, Pune 411028, INDIA

Protection from birth onwards

2301080B/3

Vacuna Conjugada Adsorbida Antidiftérica, Antitetánica, Contra la Tos Ferina, Hepatitis B y la Haemophilus influenzae tipo b

DESCRIPCIÓN

La Vacuna Conjugada Adsorbida Antidiftérica, Antitetánica, Contra la Tos Ferina, Hepatitis B y la Haemophilus influenzae tipo b, en la forma suministrada por el Serum Institute of India Pvt. Ltd., es un líquido homogéneo que contiene los toxoides purificados de difteria y tétanos, organismos inactivados de tos ferina (pertussis), partículas no-infecciosas, altamente purificadas del antígeno de superficie de la Hepatitis B (HBsAg) y el componente de Hib en la forma de una vacuna de subunidades bacterianas que contiene polisacáridos capsulares, altamente purificados, no-infecciosos de Haemophilus influenzae tipo b (Hib), químicamente conjugados a una proteína (Toxoide Tetánico). Se obtiene el antígeno de superficie del virus de la Hepatitis B (VHB) cultivando las células genéticamente manipuladas de las células de levadura de Hansenula polymorpha que tienen el gene del antígeno de superficie del virus de la Hepatitis B. El antígeno de superficie de la Hepatitis B (HBsAg) expresado en las células de *Hansenula Polymorpha*, es purificado, usando procesos de ADN recombinante, por varios pasos químicos. Se agrega el Tiomersal como preservativo.

El polisacárido de Hib se prepara del polisacárido capsular de la cepa de *H.influenzae* tipo b y después de la activación se liga al Toxoide Tetánico.

La vacuna cumple con los requerimientos de la O.M.S. y B.P. cuando se la comprueba por los métodos descritos en la O.M.S, TRS. 980 (2014), 978 (2013), 897 (2000) y BP.

Cada dosis de 0,5 ml contiene

Toxoide diftérico	⩽ 25 Lf (⩾ 30 UI)
Toxoide tetánico	⩾ 2.5 Lf (⩾ 40 UI)
B.Pertussis (de célula entera)	⩽ 16 UO (⩾ 4,0 UI)*
HBsAg (rADN)	⩾ 10 mcg
Polisacárido capsular purificado de Hib (PRP) conjugado con el toxoide tetánico (proteína transportadora)	10 mcg
Adsorbido en Fosfato de aluminio, Al^{+++}	⩽1,25 mg
Preservativo: Tiomersal	0,005%

* El límite fiducial más bajo (P=0.95) de la potencia estimada no es menos de 2,0 UI.

La Vacuna Conjugada Adsorbida Antidiftérica, Antitetánica, Contra la Tos Ferina, Hepatitis B y la Haemophilus influenzae tipo b no previene contra la Hepatitis causada por otros agentes distintos del VHB (tal como el virus A, C y E) pero es considerada efectiva en la prevención de la Hepatitis causada por el agente delta. La vacuna de Hib no protege contra las enfermedades causadas por otros tipos de *H. influenzae* ni contra la meningitis causada por otros organismos.

INDICACIONES

La vacuna conjugada, adsorbida antidiftérica, antitetánica, contra la tos ferina, hepatitis B y haemophilus influenzae tipo b está indicada para la inmunización activa de lactantes, de edad de 6 semanas o más contra la difteria, tétanos, tos ferina, hepatitis B y *Haemophilus Influenzae* tipo b.

En niños pequeños el EPI recomienda la administración de tantos antígenos como posibles en una visita única.

La Vacuna Conjugada Adsorbida Antidiftérica, Antitetánica, Contra la Tos Ferina, Hepatitis B y la Haemophilus influenzae tipo b NO debe ser usada para la dosis justo después del nacimiento.

En los países en que la tos ferina representa un peligro para los bebés recién nacidos, la vacuna de combinación debe ser iniciada en cuanto posible con la administración de la primera dosis hecha a las 6 semanas y dos dosis subsecuentes administradas en intervalos de 4 semanas.

La Vacuna Conjugada Adsorbida Antidiftérica, Antitetánica, Contra la Tos Ferina, Hepatitis B y la Haemophilus influenzae tipo b puede ser administrada segura y efectivamente simultáneamente con las vacunas de BCG, Sarampión y Poliomielitis (OPV e IPV), Fiebre Amarilla y suplementos de Vitamina A. Si se administra la vacuna La Vacuna Conjugada AdsorbidaAntidiftérica, Antitetánica, Contra la Tos Ferina, Hepatitis B y la Haemophilus influenzae tipo b simultáneamente con otras vacunas, debe ser administrada en un sitio separado. No debe ser mezclado en el frasco o jeringa con cualquier otra vacuna a no ser que cuente con la licencia para ser utilizada como un producto combinado.

POSOLOGÍA

Para la inmunización activa de bebés y niños de edad pre-escolar, se recomienda la administración de tres inyecciones intramusculares de 0,5 ml con un intervalo de cuatro semanas entre dosis. Aunque la edad normal para la primera dosis de la inmunización primaria es dos meses ahora se recomienda que se la administre a la edad de seis semanas. Se puede administrar una dosis de refuerzo de la Vacuna conjugada de DTwP y *Haemophilus Influenzae* tipo b a la edad de 15 a 18 meses.

Se debe administrar una inyección de refuerzo de la vacuna DTwP a los 5 años de edad (es decir en el momento del ingreso a la escuela).

La Academia India de Pediatría (IAP por sus siglas en inglés) recomienda que cuandoquiera estén disponibles las vacunas de combinación ellas pueden sustituir las formulaciones monovalentes indicadas en el esquema nacional de inmunización.

ADMINISTRACIÓN

No inyectar por vía subcutánea o intravenosa.

La vacuna líquida en la forma de frasco debe agitarse bien antes de usar para homogeneizar la suspensión. La vacuna debe ser inyectada intramuscularmente. No inyectar subcutáneamente o intravenosamente. El aspecto anterolateral del muslo superior es el sitio preferido de inyección, o debe ser en los músculos deltoides de niños mayores. Una inyección en las nalgas de un niño puede causar daño al nervio ciático y no es recomendada. No debe ser inyectada en la piel porque esto puede llevar a la reacción local. Una dosis pediátrica es 0,5 ml. Se debe usar una jeringa y aguja estériles para la inyección. Se debe administrar la vacuna por inyección intramuscular

Otra inyección, si administrada concomitantemente con la vacuna conjugada, adsorbida antidiftérica, antitetánica, antipertúsica, anti-hepatitis B y anti-haemophilus influenzae tipo b debe ser administrada en un sitio distinto. Se debe usar sólo agujas y jeringas estériles para cada inyección.

Una vez abiertos, los frascos multi-dosis deben ser conservados entre +2°C y + 8°C. Los frascos multi-dosis de la Vacuna Conjugada Adsorbida Antidiftérica, Antitetánica, Contra la Tos Ferina, Hepatitis B y la Haemophilus influenzae tipo b de los cuales hayan sido sacadas una o más dosis de la vacuna en el transcurso de una sesión de inmunización, pueden ser usados en sesiones subsecuentes de inmunización hasta un máximo de 28 días, a condición de que todas las condiciones se cumplan (según descrito en la declaración de política de la OMS: Manejo de frascos de vacuna multi dosis después de la apertura, OMS/IVB/14.07):

- La vacuna actualmente está precalificada por la OMS;
- La vacuna está aprobada para uso hasta 28 días después de abrir el frasco, según lo determinado por OMS;
- La fecha de caducidad de la vacuna no ha pasado;
- El frasco de la vacuna ha sido y seguirá siendo, almacenados en OMS - o fabricante de las temperaturas recomendadas; además, el sensores de control de vial de vacuna, si uno se fija, es visible en la etiqueta de la vacuna y no más allá de su punto de descarte, y la vacuna no haya sufrido daños por congelación.

La vacuna debe ser examinada visualmente para la presencia del material particulado extraño y/o variaciones en el aspecto físico antes de la administración En el evento de observar cualquier de los dos, desechar la vacuna.

CONTRAINDICACIONES

La hipersensibilidad conocida a cualquier componente de la vacuna, o una reacción severa a una dosis anterior de la vacuna combinada o cualquier de sus componentes es una contraindicación absoluta a las dosis subsecuentes de la vacuna combinada o la vacuna específica que había causado una reaccion adversa. Hay pocas contraindicaciones a la primera dosis de DTP-ataques o senales cerebrales anormales en el período postnatal inmediato o otra anormalidad neurológica sería son contraindicaciones al componente de coqueluche. En este caso no se debe administrar las vacunas como vacuna cobinada sino la vacuna DT debe administrause en lugar de DTP y las vacunas de Hepatitis B y Hib deben ser administradas saparadamente. La vacuna no perjudicará a los individuos infectados actualmente o previamente por el virus da hepatitis B.

ADVERTENCIAS

Debido al periodo largo de incubación de la Hepatitis B (hasta 6 meses o más), en los casos en que ha habido una previa exposición al virus de la Hepatitis B, puede ser que la vacunación no sea efectiva.

Si cualquier de los siguientes eventos ocurren en relación temporal a la administración de DTP, la decisión a administrar dosis subsecuentes de la vacuna que contiene el componente de tos ferina debe considerarse cuidadosamente. Puede haber circunstancias, tal como una alta incidencia de tos ferina, en las cuales los beneficios potenciales pesen más que los riesgos, particularmente dado que estos eventos no se asocian con secuelas permanentes.

- Temperatura 40,5°C (105°F) o más dentro de 48 horas de administrar una dosis, no explicada por cualquier otra causa.