Vaxtar-5™

(For Intramuscular use)

Description

DTwP-HepB-Hib [Liquid] combination **Vaxtar-5™** vaccine is a sterile, whitish turbid, uniform suspension of purified diphtheria and tetanus toxoids, inactivated whole cell pertussis, non-infectious particles of HBsAg and Hemophilus influenzae type b (Hib) Component as a bacterial subunit vaccine containing highly purified, non-infectious Hib capsular polysaccharide conjugated to a protein (tetanus toxoid). These antigens are adsorbed onto aluminium phosphate (as adjuvant) and suspended in normal saline. Thiomersal is added as preservative.

Composition

Each single dose of 0.5 mL contains:

Diphtheria toxoid:	≥30 IU (≥20 Lf to ≤30 Lf)
Tetanus toxoid:	≥60 IU (≥5 Lf to ≤25 Lf)
Inactivated whole cell *B. pertussis*:	≥4 IU
HBsAg (rDNA):	≥10 µg
Hib Polysaccharide covalently bound to TT (PRP-TT):	≥10 µg
Al^{+++} content (as $AlPO_4$ gel):	≤1.25 mg
Thiomersal (as preservative):	≤0.01% w/v
Normal saline (sodium chloride 0.9%)	q.s

Pharmaceutical Form

Vaxtar-5™ vaccine is a homogenous liquid containing purified diphtheria and tetanus toxoids, inactivated pertussis organisms, highly purified non-infectious HBsAg and Hib component.

Clinical Particulars

Therapeutic indications

Vaxtar-5™ vaccine is indicated for the active immunization of infants, at or above the age of 6 weeks, against diphtheria, tetanus, whooping cough, hepatitis B and Hib infections.

Posology and Method of Administration:

Posology

For active immunization of infants and pre-school children, it is recommended that 3 intramuscular injections of 0.5 mL be administered with an interval of 4 weeks between doses starting at 6 weeks of age. In countries where perinatal transmission of HBV is common, the first dose of hepatitis B vaccine should be given as soon as possible after birth. In this case, the combination vaccine can be used to complete the primary series starting from 6 weeks of age.

Dosage schedule:

1st dose : 6 weeks

2nd dose : 10 weeks

3rd dose : 14 weeks

Source: WHO/IAP recommended immunization schedule.

A booster dose of DTP and Hib should be given at the age of 15–18 months. A reinforcing booster dose of DTP should be administered at 5 years of age (i.e. at the time of school entry).

Administration

The liquid vaccine vial should be gently shaken before use to homogenize the suspension. The vaccine should be injected intramuscularly. Do not inject subcutaneously or intravenously. The anterolateral aspect of the upper thigh is the preferred site of injection or the deltoid muscles in case of older children. An injection into a child's buttocks may cause injury to the sciatic nerve and the absorption from this site may be erratic. Hence administration of any vaccine at this site is not recommended. It must not be injected into the skin as this may give rise to local reactions.

A sterile syringe and sterile needle must be used for the injection. The site of administration must be sterilized by cotton soaked in rectified spirit which should be allowed to evaporate before injection.

Another injection if co-administered with **Vaxtar-5™** vaccine, should be given at 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 **Vaxtar-5™** vaccine from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 6 hours, 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 the dose.

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. **Vaxtar-5™** vaccine should not be mixed with any other vaccine before injection.

Contraindications

It is contraindicated in case of known 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 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 a contraindication for further use.

Special Warnings and Special Precautions for Use

Warnings

Due to the long incubation period of hepatitis B (Up to 6 months or more), cases where prior exposure to HBV has taken place, vaccination may not be effective.

If any of the following events occur in temporal relation to receipt of **Vaxtar-5™** vaccine. The decision to give subsequent doses of vaccine containing the pertussis component should be considered carefully:

- Temperature >40.0°C (>104.0°F) 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 3 days.

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. **Vaxtar-5™** 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. Local application of ice pack by aseptic means is recommended in such conditions to minimize bleeding.

Infants and children, with a history of convulsion in first-degree family members (i.e. siblings and parents) when administered DTP containing vaccine, have an increased risk for neurologic events and permanent neurologic damage when compared with infants without such history. 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 2 or 3 days following vaccination.

The administration of **Vaxtar-5™** 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 reaction 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 **Vaxtar-5™** vaccine, healthcare personnel should inform the guardian of the child about the benefits and risks of immunization, and also inquire about the recent health status of the child to be vaccinated. Parents of a child with a family history of seizures should be informed that their child has an increased risk of seizure following administration of any DTP containing vaccine. They should be instructed regarding appropriate medical care in the unlikely event of 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 the 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 SC or IM. 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 life saving.

As with the use of all vaccines, the vaccinee should remain under observation for not less than 30 minutes for the possibility of occurrence of immediate or early allergic reactions. Hydrocortisone hydrochloride and antihistaminics should also be available in addition to supportive measures such as oxygen inhalation.

Interaction with Other Medicaments 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 immunosuppressive.

Undesirable Effects

Limited information is available on possible adverse reactions associated with **Vaxtar-5™** vaccine.

As per clinical trial data:

Local: Pain, swelling, erythema and induration at the site of injection.

Systemic: Fever, irritability, unusual crying, loss of appetite, vomiting and drowsiness.

Data from similar vaccines suggest that high fever (i.e. temperature of > 40.0°C/>104°F) and persistent, inconsolable crying lasting 3 hours or more can occur infrequently and appear to be without sequel. Sterile abscesses at the site of injection have been reported.

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 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 administration of DTP containing vaccine. An analysis of these data failed to show any cause and effect association.

Overdose

No data is available

Pharmacological Properties

Pharmacotherapeutic group: Vaccines, combined vaccines

ATC code: JO7CA11

Pharmacokinetic Properties

Not applicable

Preclinical Safety Data

Toxicology

No significant finding was observed in the preclinical toxicological studies and the vaccine was found to be safe.

Pharmaceutical Particulars

Incompatibilities

This product must not be mixed with other medicinal products.

Shelf-Life

Twenty four months from the date of manufacture, when stored in recommended storage conditions.

Special Precautions for Storage:

a) Protect from light

b) Do not freeze. Discard vial if contents are frozen.

c) Store out of reach of children.

d) **Vaxtar-5™** vaccine must be stored and transported between +2°C to +8°C.

e) If not maintained at +2°C and +8°C the vaccine must be immediately discarded.

The Vaccine Vial Monitor (VVM) has not reached the discard point.

- Inner square lighter than outer circle.
  If the expiry date has not been passed, USE the vaccine.
- At a later time, inner square still lighter than outer circle
  If the expiry date has not been passed, USE the vaccine.
- Discard point: Inner Square matches color of outer circle
  DO NOT USE the vaccine.
- Beyond the discard point:
  Inner Square darker than outer ring.
  DO NOT USE the vaccine.

Presentation

Single dose: 1 dose of 0.5 mL vial, and

Multi-dose: 10 dose vial of 5 mL.

Combo pack contains single dose of DTwP-HepB-Hib Vaccine, sterile disposable syringe with needle and alcohol swab.

Special Precautions for Disposal

Any unused product or waste material should be disposed off in accordance with local requirements for bio-waste management.

Caution

Do not use if precipitation is observed.

Schedule H Prescription Drug-Caution

Not to be sold by retail without the prescription of a registered medical practitioner.

References

https://www.ema.europa.eu/en/documents/product-information/quintanrix-epar-product-information_en.pdf

™ Trade Mark

Manufactured and Marketed by:

Human Biologicals Institute

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TETANUS

Tetanus is an acute, often fatal, disease caused by an exotoxin produced by the bacterium *Clostridium tetani*, a slender, gram-positive, anerobic rod that may develop a terminal spore.

These spores are widely distributed in soil and in the intestines and feces of horses, sheep, cattle, dogs, cats, rats, guinea pigs and chickens and are very resistant to heat and the usual antiseptics. *C. tetani* produces two exotoxins, viz.:

1. **Tetanolysin**- Having unknown function.
2. **Tetanospasmin**- The most potent toxins causing clinical manifestations of tetanus.

Pathogenesis

C. tetani usually enters the body through a wound and germinates in the presence of anaerobic conditions, producing toxins that get disseminated via blood and lymphatics within the CNS, including peripheral motor end plates, spinal cord and brain and in the sympathetic nervous system. Typical clinical manifestations of tetanus are caused when tetanus toxin interferes with release of neurotransmitters, blocking inhibitor impulses resulting in unopposed muscle contraction and spasm. Seizures may occur and the autonomic nervous system may also be affected, characterized by generalized rigidity and convulsive spasms of skeletal muscles, initially of the jaw (lockjaw) and neck and then progressing to become generalized.

Clinical Features

The incubation period ranges from 3–21 days, usually about 8 days and it is dependent on the injury site i.e. a long incubation period if further from the CNS. Chance of death is higher with a short incubation period. On the basis of clinical findings, three different forms of tetanus have been described:

1. **Local Tetanus**- Uncommon form of the disease, in which patients have persistent contraction of muscles in the same anatomic area as the injury with only about 1% cases being fatal.
2. **Cephalic Tetanus**- Rare form of the disease, occasionally occurring with otitis media following injuries to the head.
3. **Neonatal Tetanus**- Generalized tetanus occurring in new born infants.

Medical Management

Clean the wound and remove necrotic tissue and foreign material. Supportive therapy and maintenance of an adequate airway are critical in the presence of tetanic spasms.

Tetanus Immune Globulin (TIG) helps remove unbound tetanus toxin and is recommended for persons with tetanus. It cannot affect toxin bound to nerve endings. A single intramuscular dose of 3,000–5,000 units is generally recommended for children and adults, with part of the dose infiltrated around the wound if it can be identified. Intravenous Immune Globulin (IVIG) contains tetanus antitoxin and may be used if TIG is not available. Because of the extreme potency of the toxin, tetanus disease does not result in tetanus immunity. Active immunization with tetanus toxoid should begin or continue as soon as the person's condition has stabilized.

Reference

Available at: www.cdc.gov/vaccines/pubs/pinkbook/downloads/tetanus.pdf. Accessed on December 11 2014.