SUMMARY OF PRODUCT CHARACTERISTICS

Vaxtar-5™

[ATC Code: J07CA11]

December 2023

Manufactured by

HUMAN BIOLOGICALS INSTITUTE
(A Division of Indian Immunologicals Limited)
Rakshapuram, Gachibowli Post,
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Web:www.indimmune.com

1. NAME OF THE MEDICINAL PRODUCT

Brand Name: Vaxtar-5™ (Liquid)

Generic Name: Diphtheria, Tetanus, Pertussis (Whole Cell), Hepatitis B (rDNA) and *Haemophilus influenzae Type* b Conjugate Vaccine (Adsorbed)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

***Each 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 *Bordetella pertussis*	≥ 4 IU
Hepatitis B surface antigen (rDNA)	≥ 10 µg
Hib Polysaccharide covalently bound to TT (PRP-TT)	≥ 10 µg
Al^{+++} content (as $AIPO_4$ gel)	≤ 1.25 mg
Thiomersal (as preservative)	≤ 0.01% w/v
Normal saline (Sodium Chloride 0.9% w/v)	q.s.

3. PHARMACEUTICAL FORM

Sterile suspension for intramuscular injection.

4. CLINICAL PARTICULARS

4.1. 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 *Haemophilus influenzae* type b infections.

4.2. Posology and method of administration

Posology:

For active immunization of infants and preschool children, it is recommended that three intramuscular injections of 0.5 ml be administered with an interval of four weeks between doses starting at six weeks of age. In countries where perinatal transmission of Hepatitis B virus 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 staring from 6 weeks of age.

Dosage schedule:

1st dose: 6 weeks
2nd dose: 10 weeks
3rd dose: 14 weeks

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^{TM} vaccine should be given at a different site. Only sterile needles and syringes should be used for each injection.

4.3. 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.

4.4. 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 Hepatitis B virus 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 carefully considered:

- Temperature > 40.0°C (>104.0°F) within 48 hours of a dose unexplained by another cause.
- Collapse or shock-like state (hypotonic-hypo responsive 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.

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 two or three 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 patient 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 Vaxtar-5™ vaccine, health care 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 seizures following administration of any DTP containing vaccine 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 (0.1-0.5ml 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 0.01mg/ kg (0.01ml/ 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. Along with Adrenaline, Hydrocortisone hydrochloride and antihistaminics should also be available in addition to supportive measures such as oxygen inhalation.

4.5. Interaction with other medicaments and other forms of interaction

As with other intramuscular injections, use the vaccine 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

This vaccine is not indicated in pregnant and lactating women.

4.7. Effects on ability to drive and use machines

The vaccine is not indicated for adults and there has been no reported case of use of the vaccine in people driving or using machines.

4.8. Undesirable effects

Vaxtar-5™ is generally well tolerated. The following adverse events have been observed in clinical trials and during the post marketing surveillance:

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

Systemic: Fever, irritability, persistent or unusual crying, loss of appetite, vomiting, drowsiness, cold and cough.

Like with any other vaccine, allergic reactions, hypersensitivity reactions and anaphylaxis can occur rarely.

The following additional adverse events have been documented involving use of similar Pentavalent vaccines as per published literatures:

Local: Sterile abscesses at the site of injection.

Systemic: 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. 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.

4.9 Overdose

There is no reported case of overdose with Vaxtar-5^{TM} vaccine.

5. PHARMACOLOGICAL PROPERTIES

Mechanism of action:

Vaxtar-5^{TM} Vaccine, after administration, induces production of specific antibodies against Diphtheria, Tetanus, Pertussis, Hepatitis B and *Haemophilus influenzae* type b. These antibodies result in protection from the respective diseases.

Pharmacodynamic properties:

Administration of Vaxtar-5^{TM} Vaccine stimulates the immune system of the body. The immune response thus elicited includes production of protective antibodies against Diphtheria, Tetanus, Pertussis, Hepatitis B and Haemophilus influenzae type b (Hib) in the body. The immune response is considered seroprotective when if the antibody levels against diphtheria and tetanus is ≥ 0.1 IU/ml, against hepatitis b ≥ 10 mIU/ml and against Hib is ≥ 0.15 µg/ml. There is no well-established serological correlate of protection for pertussis.

A phase I/II study was conducted to assess the safety and immunogenicity of the vaccine in which Fifty-five subjects (that included 30 subjects in the age group of 16 months to 24 months and 25 subjects in the age group of two years to 5 years) were enrolled. Subjects received a single dose of the vaccine intramuscularly and were evaluated after four to six weeks.. Pain (32.7%), swelling (10.9%) and redness (7.27%) were the local adverse events reported while crying(5.45%), fever (21.8%), irritability (5.45%), loss of apettite (1.81%) and vomiting in (1.81%) were the systemic adverse reported in the study. No serious adverse event was recorded.. The post vaccination GMT for Diphtheria, Tetanus, Pertussis, Hepatitis B and Hib components were 4.39 IU/ml, 12.11 IU/ml, 9.32 EU/ml, 1565.4 mIU/ml and 10.63 µg/ml respectively.

In Phase III study, a total of 270 subjects in the age group of 6-8 weeks were enrolled. Subjects received three doses of the vaccine intramuscularly at an interval of four to six weeks between the doses. Immunogenicity was evaluated at four to six weeks after the third dose of vaccination. The post vaccination Geometric mean titres were 0.53 IU/mL, 1.31 IU/mL, 9.06 U/mL, 614.65 mIU/mL and 4.70 µg/mL for Diphtheria, Tetanus, Pertussis, Hepatitis B and Hib components respectively. The adverse events reported in the study within 30-60 minutes were local pain (15.56%), local swelling (1.11%), local erythema (4.07%), irritability (0.37%) and persistant or unusual crying (0.74%). The adverse events reported in the study were local

pain (55.19%), local swelling (23.70%), local erythema (11.48%), local induration (11.85%), fever (38.89%), irritability (27.41%), anorexia (14.44%), drowsiness (12.59%), vomiting (4.44%), persistent or unusual crying (26.30%), cold (1.85%) cough (1.11%),.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Preclinical toxicology studies of Vaxtar-5 vaccine concluded that the vaccine is safe for use at the recommended human dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Aluminium Phosphate Gel
- Thiomersal
- Normal saline (Sodium Chloride 0.9% w/v)

6.2 Incompatibilities

This product must not be mixed with other medicinal products.

6.3 Shelf life

24 months from the date of manufacture when stored in recommended storage conditions.

6.4 Special precautions for storage

- Protect from light
- DO NOT FREEZE. Discard vial if contents are frozen.
- **Store out of reach of children.**
- Vaxtar-5™ Vaccine must be stored and transported between +2°C to +8°C.
- If not maintained at +2°C and +8°C the vaccine must be immediately discarded.
- In case of vaccine vials with vaccine vial monitor (VVM) the following has to be checked for decision regarding use/ discard of the vial:

The vaccine vial monitor (VVM), has not reached the discard point. if:

✓ 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.

The vaccine vial monitor (VVM), has reached the discard point, if:

× Inner Square matches colour of outer circle

DO NOT use the vaccine.

The vaccine vial monitor (VVM), has crossed the discard point, if:

× Inner Square is darker than outer ring.

DO NOT use the vaccine.

- 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.

6.5 Nature and contents of container

Vaxtar-5™ vaccine is available as:

Single dose: 1 dose vial of 0.5 ml

Multi dose: 10 dose vial of 5.0 ml

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

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

Human Biologicals Institute
(A division of Indian Immunologicals Ltd)
Rakshapurum, Gachibowli (P.O.)
Hyderabad-500 032, Telengana, India

8. MARKETING AUTHORISATION NUMBER

02/RR/AP/2005/V/R

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of First authorization: 23.08.2017

10. DATE OF COMPILATION OF THE TEXT

December 2023