ULIVaccines, Inc.

Typhoid Vaccine (Purified Vi-capsular Polysaccharide)

Typbar

25 mcg / 0.5 mL
Solution for Injection (IM)

FORMULATION

Each 0.5 mL single dose contains:

Typhoid Vaccine (Vi-capsular Polysaccharide of *Salmonella typhi* Ty2).....25 mcg
Phenol .....0.25% w/v
Isotonic buffer solution .....q.s. to 0.5 mL

PRODUCT DESCRIPTION

Typhoid Vaccine (Purified Vi-capsular Polysaccharide) (Typbar) is a sterile solution for intramuscular use containing the purified cell surface Vi polysaccharide extracted from *Salmonella typhi* of the Ty2 strain. It also contains phenol and buffer solution (sodium chloride, disodium phosphate, monosodium phosphate and water for injection).

The vaccine appears as a clear, colorless solution in a single dose 0.5 mL USP type 1 glass vial or single dose prefilled syringe.

CLINICAL PHARMACOLOGY

Typhoid fever is an acute generalized infection caused by *Salmonella typhi*, an organism for which humans are the only reservoir. The disease affects the reticuloendothelial system, intestinal lymphoid tissue and gall bladder. It is characterized by sudden onset of sustained fever, severe headache, nausea, loss of appetite, constipation or sometimes diarrhea. Skin lesions known as rose spots may be present. Among the less common but most severe complications are intestinal perforation and hemorrhage, and death.

Salmonella typhi possesses several antigen groups (e.g., O, H, Vi). Natural infection with *S. typhi* generally confers lifelong immunity; however, the nature of this immunity is complex and includes both humoral and cell-mediated components.

Administration of Typhoid Vaccine (Vi-capsular Polysaccharide) stimulates immunity to *S. typhi* by inducing production of antibodies to the Vi capsular antigen. The Vi-antigen is considered to be a virulence factor of *S. typhi*, apparently protecting the organism from the actions of complement, and antibodies to the Vi-antigen confer protection against typhoid fever.

Immunogenicity: A study was done to evaluate the immunogenicity and safety of Typhoid Vaccine (Purified Vi-capsular Polysaccharide) (Typbar) in healthy male and female subjects (n=185) 10 to 25 years old. The vaccine was administered intramuscularly (IM) as a single 25-mcg dose. Blood samples were collected twice for immunological assessment at baseline and four weeks after the dose for antibody titer estimation. The mean antibody level on the 30th day after immunization with Typhoid Vaccine (Purified Vi-capsular Polysaccharide) (Typbar) was significantly higher compared to the pre-immunization mean antibody level (P<0.0001). The seroconversion rate on the 30th day after immunization was 71.81%. Adverse events observed include pain, redness at injection site, and rare cases of fever and headache, resolving in 48 hours with symptomatic treatment. No serious vaccine-related adverse reactions were observed. These results were comparable with the commercially available reference vaccine.

In another study involving healthy children (n=534) 2 to 15 years old, Typhoid Vaccine (Purified Vi-capsular Polysaccharide) (Typbar) was administered IM as a single 25-mcg dose. Blood samples were obtained at baseline and 28 days after vaccination. The geometric mean antibody level was significantly higher compared to the pre-immunization level (P<0.05). Seroconversion rate on the 28th day after immunization with Typhoid Vaccine (Purified Vi-capsular Polysaccharide) (Typbar) was 76.71%. The most common adverse events noted were fever and pain at injection site. These results were comparable with the commercially available reference vaccine.

INDICATION
For the active immunization against typhoid fever.

Typhoid vaccination is recommended in the following:
- Persons at risk of intimate exposure (e.g., continued household contact) to a known typhoid carrier or patient
- Food handlers such as dietary personnel, cooks, waiters, servers, dieticians, nutritionists
- Microbiology laboratory workers with frequent contact with cultures of *S. typhi*
- School-age children and young adults in areas where typhoid fever in these age groups is a significant public health problem, and particularly where antibiotic-resistant *S. typhi* strains are prevalent
- Travelers to areas where typhoid fever is endemic
- Healthcare personnel
- Police, Armed forces and such other regimented personnel

- There is no evidence to support the use of typhoid vaccine to control common source outbreaks, disease following natural disaster or in persons attending rural summer camps.
- Typhoid vaccine should not be used to treat a patient with typhoid fever or a chronic typhoid carrier.

DOSAGE AND ADMINISTRATION

- Typhoid Vaccine (Purified Vi-capsular Polysaccharide) (Typbar) is for intramuscular (IM) injection only.
  - ► In adults, IM injections of typhoid vaccine should be administered into the deltoid area.
  - ► In children, IM injections of the vaccine should be administered into the deltoid or the vastus lateralis.
- The vaccine should be administered with caution to those with thrombocytopenia or bleeding disorders since bleeding may occur after IM administration in these subjects. Following injection, firm pressure should be applied to the site (without rubbing) for at least two minutes.
- **DO NOT inject intravenously**. Typhoid Vaccine (Purified Vi-capsular Polysaccharide) (Typbar) should not be injected into the gluteal area or any area where there may be nerve trunk.
- Shake the vaccine well before use.

Immunization Schedule:
- The recommended dose for adults and children 2 years of age or older is a single dose of 0.5 mL.
- Vaccination should occur at least 2 weeks prior to potential exposure to *S. typhi* infection.
- Those who remain at risk, or who may be re-exposed to risk of typhoid fever should be given a single booster dose of vaccine every 3 years.
- Or, as prescribed by a physician.

Directions for Use:
- Prior to administration, the vaccine should be inspected visually for particulate matter and/or discoloration. In the event of either being observed, discard the vaccine.
- When using the prefilled syringe, the syringe and its packaging should also be inspected before use for evidence of leakage, premature activation of the plunger, or a faulty tip seal. If evidence of such defects is observed, the vaccine should not be used.
- Observe strict aseptic technique when handling the vaccine. If contaminated, it has the potential to become a source of infection to patients.
- The vaccine is intended for single use only and must be disposed properly and promptly following its use.
- Whenever a dose of this vaccine is administered, a record should be made of the specific type of vaccine given, manufacturer, lot number, age of the patient, and date of administration.

Incompatibilities:
- Typhoid Vaccine (Purified Vi-capsular Polysaccharide) (Typbar) should not be mixed with other vaccines or medicinal products in the same syringe.

CONTRAINDICATIONS
- Known hypersensitivity to any component of the vaccine.
- Patients who have shown signs of hypersensitivity after previous administration of typhoid vaccine.

WARNINGS AND PRECAUTIONS

- The vaccine protects against typhoid fever caused by *Salmonella typhi*. Protection is not conferred against *Salmonella paratyphi* and other non-typhoidal *Salmonellae*.
- The importance of maintaining attention to personal, food and water hygiene must be emphasized for all persons at risk of typhoid fever.
- Prior to immunization, the patient's medical history should be reviewed for possible sensitivity to the vaccine. As with any vaccine, appropriate medical treatment including epinephrine should be available for immediate use in case of an anaphylactic or hypersensitivity reaction.
- The administration of Typhoid Vaccine (Vi-capsular polysaccharide) (Typbar) should be delayed in the presence of febrile illness or acute infection except when in the opinion of the physician withholding the vaccine entails a greater risk.
- As with other IM injections, Typhoid Vaccine (Vi-capsular polysaccharide) (Typbar) should be administered with caution to individuals on anticoagulant therapy.
- It may be expected that in patients receiving immunosuppressive therapy or patients with immunodeficiency, an adequate response may not be achieved. In such cases it is recommended to postpone vaccination until the end of the disease or treatment. Nevertheless, vaccination of patients with chronic immunodeficiency such as HIV infection is recommended even if the antibody response might be limited.
- As with any vaccine, a protective immune response may not be elicited in all vaccinees.

INTERACTIONS WITH OTHER MEDICAMENTS
In general, separate injection sites must be used in case of concomitant vaccine administration.
- **Immune Globulins**: Since Typhoid Vaccine (Vi-capsular polysaccharide) is an inactivated vaccine, it can be administered simultaneously with (at a different site) or at any time before or after a dose of immune globulin.
- **Live vaccines**: Specific interaction studies involving Typhoid Vaccine (Vi-capsular polysaccharide) and other vaccines have not been conducted to date. However, since the parenteral typhoid vaccine is an inactivated vaccine, it generally can be administered simultaneously with (at a different site) or at any interval before or after live vaccines.
- **Inactivated vaccines and toxoids**: Specific drug interaction studies involving Typhoid Vaccine (Vi-capsular polysaccharide) and other vaccines commonly administered prior to international travel (e.g., tetanus, poliomyelitis) have not been conducted to date. However, since the parenteral typhoid vaccine is an inactivated vaccine, it can be administered simultaneously with (at a different site) or at any interval before or after other inactivated vaccines.
- **Other drugs**: Specific studies evaluating drug interactions involving Typhoid Vaccine (Vi-capsular Polysaccharide) and other drugs, including antimalarial and anti-infective agents, have not been conducted to date.

STATEMENT ON USAGE FOR HIGH RISK GROUPS

Pregnancy: The effect of Typhoid Vaccine (Purified Vi-capsular Polysaccharide) (Typbar) on fetal development or reproduction capacity has not been evaluated. The vaccine should be administered in pregnant women only if clearly needed.

Lactation: It is not known if Typhoid Vaccine (Purified Vi-capsular Polysaccharide) (Typbar) is excreted in human milk. The vaccine should be administered during breastfeeding only if clearly needed.

Children: The safety and efficacy of Typhoid Vaccine (Purified Vi-capsular Polysaccharide) (Typbar) in children younger than 2 years of age has not been established. As with other polysaccharide vaccines, the antibody response may be inadequate in this age group. Therefore, the decision to use the vaccine in children below 2 years old should be based upon the risk of exposure to disease.

UNDESIRABLE EFFECTS

In general, most adverse events (AEs) associated with Typhoid Vaccine (Vi-capsular Polysaccharide) are mild and transient local reactions and rarely persist longer than 48 hours.

The following AEs information is derived from clinical trials and post-marketing surveillance (PMS) studies.

Data from Clinical Trials

General disorders/Local reactions: Pain, soreness/swelling, erythema/redness, and induration at injection site, tenderness (e.g., pain on direct pressure); pruritus/itching, rash, urticaria, and paresthesia/tingling have also been reported

Systemic effects: Fever, headache, malaise, generalized aches, myalgia/muscle aches, nausea, diarrhea, vomiting, feverishness (subjective assessment), rigors/chills, sweating, decreased activity/lethargy; respiratory tract symptoms also have been reported in a few individuals receiving the vaccine.

The type and severity of AEs reported in children are similar to those reported in adults. Moreover, the frequencies of adverse systemic effects after booster dose are similar to those reported following the first dose.

Serious or life-threatening systemic AEs have not been reported following administration of Typhoid Vaccine (Vi-capsular Polysaccharide) in controlled clinical studies.

Data from Post-marketing Studies

These AEs have been very rarely reported; however, because they were voluntarily reported from a population of uncertain size, it is not always possible to reliably calculate their frequencies or to establish a causal relationship to Typhoid Vaccine (Vi-capsular Polysaccharide) exposure.

General disorders: Asthenia, fatigue, flu-like episode, lymphadenopathy, excessive crying, loss of appetite

Dermatologic/Hypersensitivity reactions: Anaphylactic/anaphylactoid reactions, including shock; serum sickness; allergic-type reactions such as difficulty breathing and hypotension

An allergic-type reaction consisting of sweats, myalgia, and difficulty of breathing occurred within 2 hours of an IM injection of Typhoid Vaccine (Vi-capsular Polysaccharide) in a woman who had a history of multiple allergies and had previously received 2 complete series of typhoid whole-cell vaccine.

Musculoskeletal and connective tissue disorders: Arthralgia, cervical pain

Nervous system: Loss of consciousness, tremor, irritability

Gastrointestinal: Abdominal pain

Respiratory: Asthma, common cold

Other Adverse events: Glomerulonephritis, neutropenia, bilateral retinitis, and polyarthritis have been reported in patients who had also received other vaccines; however a causal relationship to Typhoid Vaccine (Vi-capsular Polysaccharide) has not been established.

OVERDOSE AND TREATMENT

The symptoms reported during overdose are similar to those reported following normal dosage of Typhoid Vaccine (Vi-capsular Polysaccharide) [see **Undesirable Effects**].

STORAGE CONDITIONS
- Store at temperatures between 2-8°C.
- Do not freeze. Discard if frozen.
- Keep the product out of sight and reach of children.

AVAILABILITY:

Box of 1's (pre-filled syringe)

CAUTION: Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

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