For use only of a Registered Medical Practitioner or Hospital or Laboratory

Typhoid (Vi Capsular Polysaccharide)- Tetanus Toxoid Conjugate Vaccine

Typbar TCV®

1. NAME AND DESCRIPTION OF THE MEDICINAL PRODUCT

Typbar-TCV™ is a sterile, clear and colorless liquid containing purified Vi capsular polysaccharide of *Salmonella typhi* Ty2 which is conjugated to Tetanus Toxoid carrier protein.

This is T-cell dependent which induces Vi antibodies that neutralize Vi antigen unlike T-cell independent plain Vi polysaccharide vaccines.

Typbar-TCV™ can be administered to infants of age ≥ 6 months, children and adults as a single dose intramuscularly.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

For single dose (0.5 mL)
Each 0.5 mL of dose contains:

Purified Vi-Capsular Polysaccharide of *S. typhi* Ty2 conjugated to Tetanus Toxoid	25 µg
Sodium chloride	4.5 mg
Water for Injection (WFI)	q.s. to 0.5 mL

For multi dose (2.5 mL)
Each 0.5 mL dose contains:

Purified Vi-Capsular Polysaccharide of *S. typhi* Ty2 conjugated to Tetanus Toxoid	25 µg
Sodium chloride	4.5 mg
2-Phenoxyethanol	5 mg
Water for Injection (WFI)	q.s. to 0.5 mL

3. PHARMACEUTICAL FORM

A clear, colorless liquid for intramuscular injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Typbar-TCV™ is indicated for active immunization against *salmonella typhi* infection in adults, children and infants of age ≥ 6 months and above.

4.2 Posology and Method of Administration

Inject 0.5 mL intramuscularly. **Typbar-TCV™** should be given intramuscularly in the deltoid or the vastus lateralis of children below two years of age. **Typbar-TCV™** should not be injected into the gluteal areaor areas where there may be a nerve trunk. Prevention becomes effective in 2-3 weeks after immunization.

4.3 Dosage & Schedule

The immunizing dose for adults, children and infants of age ≥6 months is single dose of 0.5 mL; a booster dose may be given after 3 years.

4.4 Contraindications

Hypersensitivity to any constituent of the vaccine.
- Pregnant & lactating women.
- In the event of fever or severe infection.

4.5 Special Warning/ Precautions

- Do not administer intravenously, intradermally, or subcutaneously.
  Typbar-TCV™ protects against typhoid fever caused by *Salmonella typhi*. Protection is not conferred against Salmonella Paratyphi and other non-typhoidal *Salmonellae*.

  Vaccine should be visually checked for the presence of any particulate matter. Do not use the contents of the vial if in doubt and discard it.
  Epinephrine injection (1:1000) must be immediately available in case of an acute anaphylactic reaction or any allergic reaction occurs due to any component of the vaccine. The vaccinee should remain under medical supervision for not less th an 30 minutes after vaccination.Like all other vaccines, supervision and appropriate medical treatment should always be available to treat any anaphylactic reactions following immunization.
  Typbar-TCV™ should not be mixed with other vaccines or medicinal products in the same syringe.

4.6 Interaction with other medicinal products/ other forms of interaction

For concomitant or co-administration use different injection sites and separate syringes. **Typbar-TCV™** should not be mixed with any other vaccine or medicinal product, because the interactions with other vaccines or medical products have not been established.

4.7 Pregnancy and Lactation

Safety and effectiveness have not been established in pregnant women and in nursing mothers. It is not known whether this vaccine is excreted in human milk.

4.8 Effect on ability to drive and use machines

No studies on the effect of **Typbar-TCV™** on the ability to drive and use machines have been performed.

4.9 Undesirable Effects

The safety of **Typbar-TCV™** vaccine was established in a controlled clinical trial in infants ≥ 6 months to 2 years, in children and adults in the age group of and >2 to 45 years.

Within each system organ class the adverse reactions were ranked under headings of frequency using the following convention:

Very common	: ≥ 10%
Common	: ≥ 1% and < 10%
Uncommon	: ≥ 0.1% and < 1%
Rare	: ≥ 0.01% and < 0.1%
Very rare	: < 0.01%

Data from clinical studies

A total of 981 healthy subjects were enrolled into the study at 8 clinical sites. There were 2 cohorts in the study, cohort-I was single arm open label and 327 subjects were recruited between the age of ≥ 6 months to 2 years. All the subjects received single dose of **Typbar-TCV™** vaccine. The cohort-II was randomized double blind trial and 654 subjects between the age >2 years to 45 years were recruited who received single dose of either **Typbar-TCV™** or comparator vaccine.

The most frequently reported Adverse Events after administration of **Typbar-TCV™** were fever and pain at injection-site. These usually occurred within the first 4 8 hours after vaccination and disappeared within 2 days.

General and administration site conditions

Common: Fever, pain at injection site and swelling
Uncommon: Tenderness, Itching, Arthralgia, Cold, Cough, Vomiting and Myalgia

4.10 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Typhoid fever is a very common and serious bacterial disease caused by *Salmonella typhi*. All conjugate vaccine studies have shown that the efficacy and immunogenicity are higher than the plain Vi polysaccharide vaccine. In the manufacturing of **Typbar-TCV™**, the Vi polysaccharide has been conjugated with nontoxic Tetanus Toxoid. This innovative vaccine has a higher immunogenicity response and is T-cell dependent which induces Vi antibodies that neutralize Vi antigen and hence prevents the infection.

5.2 Clinical Studies

During Phase III clinical study, after a single dose of **Typbar-TCV™**, percentage of seroconversion (≥ 4-fold titer rise) in subjects between ≥ 6 months to 2 years, >2 to 15 years and >15 to 45 years were obtained as 98.05%, 99.17% & 92.13% respectively.

5.3 Pharmacokinetic Properties

Evaluation of pharmacokinetic properties is not required for vaccines.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Sodium chloride
- 2 -Phenoxyethanol (in multi dose vials)

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products.

6.3 Shelf Life

2 years from the date of manufacture.

6.4 Special Precautions for Storage

Store in a refrigerator at 2° to 8°C (35° to 46°F).

DO NOT FREEZE. DISCARD IF FROZEN.
KEEP OUT OF REACH OF CHILDREN.

Do not use the vaccine after the expiration date shown on the label. Opened vial should be used within 6 hrs when stored under refrigeration at 2° to 8°C (35° to 46°F). For multi dose vials use different syringe each time to vaccinate.

7. PRESENTATION

Typbar-TCV™ is presented in USP type 1 glass vial and Pre Filled Syringes

Single dose	: 0.5 mL
Single dose PFS	: 0.5 mL
Multi dose	: 2.5 mL

WARNING: To be sold by retail on the prescription of a Registered Medical Practitioner only.

Manufactured & Marketed by:

Bharat Biotech International Ltd.,
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Andhra Pradesh, India.