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

Typhoid Vi Conjugate Vaccine I.P.

Typbar TCV®

1. NAME AND DESCRIPTION OF THE MEDICINAL PRODUCT

Typbar-TCV™ is a clear to slightly turbid 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 to ≤ 45 years, children and adults as a single dose intramuscularly. The vaccine full fills WHO requirements for Typhoid Vi Conjugate vaccine.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

For single dose (0.5 mL)

Each dose of 0.5 mL contains:

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

For multi dose (2.5 mL)

Each dose of 0.5 mL contains:

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

3. PHARMACEUTICAL FORM

Suspension for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Typbar-TCV™ is indicated for active immunization against *salmonella typhi* infection in ≥6 months to ≤45 years age group.

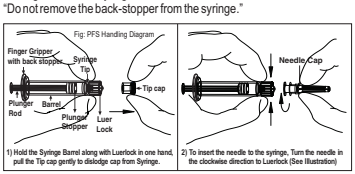
4.2 Posology and Method of Administration

Inject 0.5 mL intramuscularly. **Typbar-TCV™** should be given intra muscularly in the deltoid or the vastus lateralis of subjects. **Typbar TCV™** should not be injected into the gluteal area or areas where there may be a nerve trunk. Prevention becomes effective in 2-3 weeks after immunization.

PFS Handling procedure

Prior to administration, ensure that the plunger rod is firmly attached to the rubber stopper by turning the plunger rod clockwise until slight resistance is felt. Do not over tighten. Remove rubber tip-cap from the syringe and fix the needle on syringe by turning in clock wise direction into luer lock until it is securely fixed to the syringe, remove the needle cap before injecting. Do not rotate luer lock. Finger grip with back stopper will prevent Plunger rod coming out from the syringe Barrel.

"Do not remove the back-stopper from the syringe."



4.3 Dosage & Schedule

The immunizing dose for adults, children and infants of age ≥6 months to ≤ 45 years 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* Ty2. Protection is not conferred against Salmonella Paratyphi and other non-typhoidal *Salmonellae*.
- 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 than 30 minutes after vaccination.Like all other vaccines, supervision and appropriate medical treatment should always be available to treat any anaphylactic reactions following immunization.

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.

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 Adverse reactions

Clinical trial experience

The safety of **Typbar-TCV™** vaccine was established in phase II and III clinical trials.

Within each system organ class the adverse reactions were ranked under headings of frequency of occurrence 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%.

In the phase II study conducted in India with 100 children aged 2-17 years, no significant adverse events were demonstrated to be associated with the vaccine. Commonly reported adverse events included pain at injection site, swelling, fever and headache.

In the larger phase III study, a total of 981 healthy subjects were enrolled into the study at 8 clinical sites into 2 study cohorts. A single arm, open label cohort enrolled 327 subjects between the ages of ≥6 months to 2 years to receive a single dose of **Typbar-TCV™**. A second randomized controlled arm recruited 654 subjects between the age >2 years to 45 years, allocated equally to receive a single dose of either **Typbar-TCV™** or comparator Vi polysaccharide vaccine.

The most common general and local adverse events were fever (5-10%) and pain at injection site (2-3%) post vaccination. All these events were resolved within 48 hours with symptomatic treatment. Uncommon adverse events observed were itching, swelling, malaise and myalgia. No differences were observed in the adverse events reported between plain Vi polysaccharide and **Typbar-TCV™**. The adverse events reported were similar in nature as reported with other commercial Vi vaccines. No vaccine-related serious adverse events (SAEs) were reported in the clinical trial.

4.10 Immune response

Typhoid fever is a common and serious infection caused by Salmonella typhi bacteria. In previous published studies, conjugate vaccines have shown higher immunogenicity than the plain Vi polysaccharide. The phase III clinical trial enrolled a total of 981 healthy subjects into the trial across two age cohorts. A total of 654 subjects, aged >2 to <45 years were enrolled into a randomized controlled cohort to receive a single dose of **Typbar-TCV™** or Vi polysaccharide vaccine. 327 subjects aged >6 months to <2 years enrolled into an open label cohort all received a single dose of **Typbar-TCV™** vaccine.

After a single dose of the vaccine, seroconversion (≥4-fold increase of anti-Vi IgG antibodies) at 6 weeks post-vaccination in subjects aged 6 months to < 2 years, >2to <5 years, >5 to <15 years and >15 to <45 years was 98%, 98%, 99% and 92%, respectively. Two years after vaccination, seroconversion in the listed age groups was, 60%, 77%, 75% and 71%, respectively. In addition, anti-Vi titres remained higher in **Typbar-TCV™** subjects, were of higher avidity and supported strong booster responses in both age groups, compared to Vi polysaccharide recipients, at two years after vaccination.

4.11 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 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

The expiry date of the vaccine is indicated on the label and carton of the product

6.4 Special Precautions for Storage

Store at +2°C to +8°C

Do not freeze. Discard if frozen. Shake well before use.

Protect from light. 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 hours when stored at +2°C to +8°C. 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 Vial	: 0.5 mL
Single dose PFS	: 0.5 mL
Multi dose Vial	: 2.5 mL

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

5-PI-D.02

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