Summary of Product Characteristics (SmPC)

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 carrier protein, Tetanus Toxoid. 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 to age ≥ 6 months to ≤ 45 years, children and adults as a single dose intramuscularly. The vaccine full fills WHO requirement for Typhoid Vi Conjugate vaccine.

Brand Name: **TYPBAR TCV®**

Generic Name: Typhoid Vi conjugate vaccine

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 BP……... 4.5 mg
Water for injection BP…… q.s. to 0.5 mL

For multi dose (2.5 mL)

Each 0.5 mL of dose contains:

Purified Vi-Capsular Polysaccharide of
S. typhi Ty2 conjugated to Tetanus Toxoid ……25 µg
Sodium chloride BP……... 4.5 mg
2-Phenoxyethanol BP…… 5.0 mg
Water for injection BP…… q.s. to 0.5 mL

Pharmaceutical Dosage Form

Suspension for Injection

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Clinical Particulars

Therapeutic indications:

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

Posology and Method of administration:

Inject 0.5mL intramuscularly. **Typbar TCV®** should be given intramuscularly 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 of immunization.

Dosage and 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.

Contraindications:

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

Special warnings and precautions for use:

- 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 anaphylactic reaction or any allergic reaction occurs due to any component of the vaccine. The vaccine should remain under medical supervision for not less than 30 minutes after vaccination. Like all other vaccine, supervision and appropriate

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medical treatment should always be available to treat any anaphylactic reaction following immunization.

Interaction with other medicinal products and 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 medical product because the interaction with other vaccines or medical product has not been established.

Pregnancy and Lactation:

Safety and effectiveness have not been established in pregnant women and in nursing mothers.

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.

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 heading 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%

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

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In the large 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 ≥ 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 **Typbar TCV®** or a comparator **Vi** polysaccharide vaccine.

The most common general adverse events were fever (4-10%) and pain (3-4%) and swelling (1-2%) at injection site, post vaccination. All these events were resolved within 48 hours with symptomatic treatment. Uncommon adverse events observed were tenderness, and erythema at injection site, arthralgia, 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 event's (SAEs) were reported in the clinical trial.

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 trial across two age cohorts. A total of 654 subjects aged > 2 years 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 open label cohort all vaccine, seroconversion at 6 weeks post-vaccination in subjects aged 6 months to <2 years, >2 to <5 years, >5 to <15 years and >15 to <45 years was 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, and were higher avidity and supported strong booster responses in both age groups, compared to Vi polysaccharide recipients, at two years after vaccination.

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Overdose:

No case of overdose has been reported.

Pharmacological Properties

Pharmacodynamic properties:

Typhoid fever is a very common and serious bacterial disease cause 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 non-toxic 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.

Pharmacokinetic properties:

Evaluation of pharmacokinetic properties is not required for vaccines.

Pharmaceutical Particulars

List of excipients:

Sodium chloride

2-Phenoxyethanol (in multi dose vials)

Incompatibility:

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

Shelf life:

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

Special precautions for storage:

Store at +2º to +8ºC. Do not freeze. Discard if frozen. Shake well before use. Keep out of reach out children. Keep out of reach of children. Do not use the vaccine after the expiration date shown on the label. Opened vial should be used

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within 6 hours when stored at +2º to +8ºC. For the multi dose vials use different syringe each time to vaccinate.

Presentation

Typbar TCV is presented in USP Type 1 glass vial

Single dose vial : 0.5 mL

Multi dose (5 doses) vial : 2.5 mL

The Vaccine Vial Monitor

Vaccine Vial Monitor (VVM30) are on the cap of **Typbar TCV®** Vials supplied through Bharat Biotech. VVM30 are supplied by TEMPTIME Corporation, USA. The colour dot which appears on the cap is a VVM30. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exported. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

Marketing Authorization Holder

Name of the Company : Bharat Biotech International Limited

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Marketing Authorization Number(s)

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Category for Distribution:

Vaccine (Prescription only Medicine)

Date of First Authorization/ Renewal of the Authorization

Date of First Authorisation : 17th May 2013

Date of Renewal of the Authorisation : 1st January 2017

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