SUMMARY OF PRODUCT CHARACTRISTICS

1. NAME OF THE MEDICINAL PRODUCT

Typhoid (Vi Capsular Polysaccharide)-Tetanus Toxoid Conjugate Vaccine.

'**Typbar-TCV'**

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Qualitative Formula per dose of 0.5 mL (Single Dose Vial & PFS):

S. No.	Ingredient	Monograph
1.0	Purified Vi Capsular Polysaccharide of S. *typhi* Ty2 conjugated to Tetanus Toxoid	IH
2.0	Sodium chloride	USP
3.0	WFI	IP/BP/USP

Qualitative Formula per dose of 0.5 mL (Multi Dose Vial):

S. No.	Ingredient	Monograph
1.0	Purified Vi Capsular Polysaccharide of S. *typhi* Ty2 conjugated to Tetanus Toxoid	IH
2.0	2-Phenoxyethanol	USP
3.0	Sodium chloride	USP
4.0	WFI	IP/BP/USP

Quantitative Formula per dose of 0.5mL for Single Dose Vial & PFS:

S. No.	Ingredient	Quantity per dose
1.0	Purified Vi Capsular Polysaccharide of S. *typhi* Ty2 conjugated to Tetanus Toxoid	25 µg
2.0	Sodium chloride	4.5 mg
3.0	WFI	q.s to 0.5 mL

Quantitative Formula per dose of 0.5mL for Multi Dose vial:

S. No.	Ingredient	Quantity per dose
1.0	Purified Vi Capsular Polysaccharide of S. *typhi* Ty2 conjugated to Tetanus Toxoid	25 µg
2.0	2-Phenoxyethanol	5 mg
3.0	Sodium chloride	4.5 mg
4.0	WFI	q.s to 0.5 mL

3. PHARMACEUTICAL FORM

Typbar-TCV is liquid vaccine presented in single and multi-dose vial & single dose as Pre Fill Syringe.

Category: Active Immunizing Agent.

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

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 area or areas where there may be a nerve trunk. Prevention become effective after 2-3 weeks after immunization.

4.3 Contraindications

Typbar-TCV is contraindicated in person having Hypersensitivity to any constituent of the vaccine, Pregnant and lactating women and in the event of fever or severe infection.

4.4 Special warnings and precautions for use

- **Typbar-TCV** shall be administered by recommended route of administration i.e. intramuscular and should not be administered intravenously, intradermally or subcutaneously.
- **Typbar-TCV** protects against typhoid fever caused by *Salmonella typhi*. Protection in not conferred against Salmonella paratyphi and other non-typhoidal *Salmonellae*.
- Do not administer the vaccine if particulate matter is observed.
- 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. Vaccinee should remain under medical supervision for not less than 30 minutes after vaccination.
- **Typbar-TCV** should not be mixed with other vaccines or medicinal products in the same syringe.

4.5 Interaction with other medicinal products and other forms of interaction

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

4.6 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.

4.7 Effects 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.

4.8 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 age group of and > 2 to 45 years.

Within each system organ class the adverse reactions were ranked under headings of frequency using 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 ≥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 48 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.

4.9 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.

Clinical studies

During Phase III clinical study, after a single dose of **Typbar-TCV** percentage of seroconversion (≥ 4 fold titre 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% and 92.13% respectively.

5.2 Pharmacokinetic properties

Evaluation of Pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

The expected toxicity symptoms for vaccine include local reaction at the site of injection, pyrogenicity, anaphylactic reactions. During single and repeat dose toxicity studies, the animals were observed daily for various clinical signs and none of the animals showed any clinical signs indicative of toxicity, viz. local reactions at the site of injection, pyrogenicity and anaphylaxis. Preclinical studies showed that the vaccine was non-toxic and safe.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

- Sodium chloride and
- 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 when stored at +2° C to +8°C.

6.4 Special precautions for storage

- Do not use the vaccine after expiry date.
- Vaccine vials should be stored between +2^{o}C to +8^{o}C**.**
- Opened vial should be used with in 6 hrs when stored at +2^{o}C to +8^{o}C.
- Do not freeze. Discard if frozen.
- Keep out of the reach of children.

6.5 Nature and contents of container

Typhoid (Vi Capsular Polysaccharide)-Tetanus Toxoid Conjugate Vaccine is filled as single dose in vial/PFS and multidose in vial.

Vial:

Single dose of 0.5 mL filled in 2.0 mL USP Type-1 glass vial with a bromobutyl rubber stopper and capped with flip-off aluminium seals.

2.5 mL (5 doses of 0.5 mL/dose) filled as multi-dose in 3 mL USP Type-1 glass vial with a bromobutyl rubber stopper and capped with flip-off aluminium seals.

Pre Fill Syringe

Single dose of 0.5 mL filled in USP Type-1 glass pre-filled syringes of 1.0 mL with a butyl rubber plunger stopper.

6.5 Special precautions for disposal

Discard the vaccine if particulate matter observed.

7. MARKETING AUTHORIZATION PREQUALIFICATION HOLDER

Name of the Company: Bharat Biotech International Limited

Address:

Genome Valley, Shameerpet Mandal,

Hyderabad, Andhra Pradesh,

INDIA – 500078.

Phone No.: +91-40-2348 0567.

Fax No.: +91-40-2348 0560.

E. Mail: info@bharatbiotech.com

Web: www.bharatbiotech.com

8. MARKETING AUTHORIZATION NUMBER(S)

Marketing authorization No. MF-244/2012

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION

We got market authorization on 20.12.2012.