



Summary of Product Characteristics (SPC)

Drug Product : Typhoid Vi Conjugate Vaccine
(Typhoid Conjugate Vaccine (Monovalent))

Trade Name : TYPHIBEV



Marketing Authorisation Holder:

Plot No. 1, Biotech Park, Phase-II, Kolthur Village, Shameerpet Mandal,
Medchal-Malkajgiri District, Telangana State, INDIA – 500078

Registered Office:

18/1&3, Azamabad, Hyderabad – 500020, India.

1. NAME OF THE MEDICINAL PRODUCT

Name of Medicinal Product:	Typhoid Vi Conjugate Vaccine (Typhoid Conjugate Vaccine (Monovalent))
Trade Name:	TYPHIBEV
Presentation:	Single dose vial of 0.5 mL Five dose vial of 2.5 mL

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
COMPOSITION

Each dose of 0.5 mL contains:

Typhoid Vi Polysaccharide ¹	: 25 µg
conjugated to 16.7µg to 100µg of CRM ₁₉₇	
Sodium chloride and phosphate buffer	: q.s
2-Phenoxyethanol (as Preservative)	: 5 mg

¹Produced from *C. freundii sensu lato* 3056

For a full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Solution for Intramuscular Injection.

Typhoid Vi Conjugate Vaccine (TCV) is a clear, colourless liquid with no visible particles. The vaccine contains 25 µg of Typhoid Vi polysaccharide conjugated to CRM₁₉₇. The polysaccharide is manufactured using *Citrobacter freundii sensu lato* 3056 (Vi) and is conjugated to CRM₁₉₇ as a carrier protein. Sodium Chloride and Phosphate Buffer are used as a diluent (buffering agent) in vaccine formulation. 2-Phenoxyethanol is added as a preservative.

The conjugation of Vi polysaccharide antigen to carrier protein transforms the antigen into a T-cell dependent antigen, capable of inducing an immunological memory and an adequate immune response even in infants and younger children less than 2 years.

4. CLINICAL PARTICULARS**4.1 Therapeutic indications:**

Typhoid Vi Conjugate Vaccine is indicated for active immunization against infection caused by *Salmonella typhi* in infants, children, adolescents and adults aged ≥ 6 months to ≤ 45 years.

4.2 Posology and method of administration:**4.2.1 Posology**

BE's Typhoid Vi Conjugate Vaccine can be administered in single 0.5 mL intramuscular dose to infants, children, adolescents and adults aged ≥ 6 months to ≤ 45 years. The vaccine meets requirements of I.P. and WHO.

4.2.2 Paediatric population

A single 0.5mL dose to be given intramuscularly to infants, children, adolescents and adults.

4.2.3 Method of Administration

A single 0.5mL dose of the vaccine should be administered intramuscularly in the deltoid muscle of upper arm if muscle mass is adequate for children 2 years and above, adolescents and adults. For infants and toddlers aged ≥ 6 months to < 2 years of age, the vaccine should be administered intramuscularly in the vastus lateralis muscle on anterolateral aspect of thigh. This vaccine should not be injected into the gluteal area or in any areas where there may be a nerve trunk. Prevention becomes effective in 2-3 weeks after immunisation.

4.3 Contraindications:

- Hypersensitivity to any component of vaccine
- Pregnant & lactating women
- In case of fever and severe infection

4.4 Special Warnings and Precautions for use:

- Do not administer intravenously, intradermally or subcutaneously.

- Typhoid Vi Conjugate Vaccine protects against typhoid fever caused by *Salmonella typhi*. Protection is not conferred against *Salmonella paratyphi* and other non *typhoidal Salmonellae*.
- Adrenaline (epinephrine) injection, 1:1000 (1 mg/mL) must be immediately available in case of an acute anaphylactic reaction or any allergic reaction occurs due to any component of the vaccine. If there is no clinical improvement, the dose given may be repeated after about five minutes. In some cases, several doses may be needed, particularly if improvement is transient. 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.
- Biological E's Typhoid Vi Conjugate Vaccine 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 administration use different injection sites and separate syringes. Biological E's Typhoid Vi conjugate vaccine should not be mixed with any other vaccine or medicinal product, because the interactions with other vaccines or medical products have not been established.

4.6 Pregnancy and Lactation:**4.6.1 Women of childbearing potential**

No studies have been performed

4.6.2 Contraception in males and females

No studies have been performed

4.6.3 Pregnancy

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

4.6.4 Breast feeding

It is not known whether the vaccine is excreted in human milk.

4.6.5 Fertility

No studies have been performed

4.7 Effect on ability to drive and use machines

No studies on the effect of Biological E's Typhoid Vi conjugate vaccine on the ability to drive and use machines have been performed.

4.8 Undesirable Effects:

The safety of Biological E's Typhoid Vi conjugate vaccine was established in a controlled clinical trial in infants ≥ 6 months to < 2 years, in children, adolescents and adults of ≥ 2 years to 64 years.

Within each system organ class (SOC) the adverse reactions were ranked under headings using the following convention:

Very common	: $\geq 10\%$
Common	: $\geq 1\%$ and $< 10\%$
Uncommon	: $\geq 0.1\%$ and $< 1\%$
Rare	: $\geq 0.01\%$ and $< 0.1\%$
Very rare	: $< 0.01\%$.

4.9 Overdose:

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES**5.1 Pharmacodynamic Properties**

5.1.1 Pharmacotherapeutic group

Group: Bacteria

ATC Code: J07AP03

5.1.2 Mechanism of action

The conjugation of Vi polysaccharide antigen to carrier protein transforms the antigen into a T-cell dependent antigen, capable of inducing an immunological memory and an adequate immune response even in infants and younger children less than 2 years.

5.1.3 Pharmacodynamic effects

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 those of the plain Vi polysaccharide vaccine. In the manufacturing of Biological E's Typhoid Vi conjugate vaccine, the Vi polysaccharide is conjugated with carrier protein CRM₁₉₇. This vaccine has a higher immunogenicity response and is T-cell dependent which induces Vi antibodies that neutralize Vi antigen and hence prevents the infection.

5.1.4 Clinical efficacy and safety

The safety of Biological E's Typhoid Vi conjugate vaccine was established in the clinical trials conducted in India.

In a randomised comparative licensure study, a total of 622 healthy subjects were enrolled at nine clinical sites into one of the two treatment arms. 311 subjects are enrolled in each treatment arm and received a single 0.5mL dose of either Biological E's Typhoid Vi Polysaccharide Vaccine or a comparator vaccine. All subjects were further stratified into 3 age subsets viz., ≥ 6 months to < 2 years, ≥ 2 years to < 18 years and ≥ 18 years to < 64 years of age, for comparison under each arm.

The most frequently reported local adverse events after administration of Biological E's Typhoid Vi Conjugate vaccine were Injection Site Pain (4.50%), Injection Site erythema (0.64%) and Injection site.

Swelling (0.32%). These usually occurred within first 48 hours and disappeared within 2-3 days.

The most frequently reported systemic adverse events were Pyrexia (2.25%), Vomiting (0.96%), Headache (0.64%), Fatigue (0.64%), Arthralgia (0.32%) and Rash (0.32%). No vaccine-related serious adverse events (SAEs) were reported in the clinical trial.

General and administration site conditions:

- Common: Pain, Swelling and Erythema at injection site, Fatigue and Fever.

Skin and Subcutaneous Tissue:

- Uncommon: Rash.

Nervous system Disorder:

- Uncommon: Headache

Musculoskeletal and Connective tissue disorders:

- Uncommon: Arthralgia

Gastrointestinal Disorders

- Uncommon: Vomiting

Immune Response:

Overall (≥ 6 months to < 64 years) with Biological E's Typhoid Vi conjugate vaccine, it was observed that the proportion of subjects with anti-Vi IgG antibody concentrations above the short term protective seroconversion threshold value of ≥ 2.0 $\mu\text{g/mL}$ and above the long-term protective seroconversion threshold value of ≥ 4.3 $\mu\text{g/mL}$ were 98.98% and 95.59% respectively. The seroconversion rates in ≥ 6 months to < 2

years, ≥ 2 years to < 18 years and ≥ 18 years to < 64 years of age were 99.22%, 100.0% and 97.62% using the short-term threshold value of ≥ 2.0 $\mu\text{g/mL}$ and 96.90%, 95.12% and 94.05% using long-term threshold value of ≥ 4.3 $\mu\text{g/mL}$ respectively. Overall, the proportion of subjects achieving ≥ 4 fold increase in anti-Vi IgG antibody concentrations at day 42 from pre vaccination were 96.95%.

5.1.5 Paediatric population

The clinical studies were conducted to evaluate immunogenicity and safety of single intramuscular dose of Biological E's Vi-capsular Polysaccharide-CRM₁₉₇ Conjugate Typhoid Vaccine in healthy infants, children and adults aged ≥ 6 months to < 64 years.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines

5.3 Preclinical safety data

Single dose toxicity studies in Rats and repeat dose toxicity studies in Rats and Rabbits were conducted. Based on the toxicity studies conducted, it is concluded that the vaccine formulation did not produce any adverse effects at dose level of 0.5 mL.

Immunogenicity studies are also conducted with the vaccine in Rats and Rabbits. Based on the immunogenicity studies, the vaccine showed IgG response in the vaccine formulation.

6. Pharmaceutical Particulars:

6.1 List of Excipients:

- Sodium chloride and Phosphate Buffer
- 2-Phenoxyethanol (Preservative)

6.2 Incompatibilities

This vaccine must not be mixed with other medicinal products.

6.3 Shelf Life:

2 years from the date of manufacturing. The expiry date of the vaccine is indicated on the label and carton of the product.

6.4 Special precaution for storage:

Store at +2°C to +8°C (35.6°F to 46.4°F). DO NOT FREEZE.

Discard if found frozen. Shake well before use. Keep out of reach of children.

6.5 Nature and contents of the container

BE's Typhoid Vi conjugate vaccine is offered in the following presentations:

- Single dose of 0.5 mL filled in 3 mL USP Type 1 glass vials
- Multi dose of 2.5 mL filled in 3 mL USP Type 1 glass vials

6.6 Special precautions for disposal and other handling:

Each vaccine dose of 0.5 mL is withdrawn into a syringe for injection to be administered intramuscularly. Use a separate sterile needle and syringe for each individual. It is normal for liquid to remain in the vial after withdrawing the final dose.

When low dead volume syringes and /or needles are used, the amount remaining in the vial may be sufficient for an additional dose. Care should be taken to ensure to full 0.5 mL dose is administered. Where a full 0.5 mL dose can not be extracted, the remaining volume should be discarded. Do not pool excess vaccine from multiple vials.

Aseptic technique should be used for withdrawing the dose for administration.

Handling of multi dose vial:

Once opened, multi dose vials of BioE's Typhoid Vi conjugate vaccine from which one or more doses of vaccine have been removed during an

immunization session may be used in subsequent immunization sessions for up to a maximum of 28 days, provided that all of the following conditions are met:

- the expiry date has not passed
- the vaccines are stored under appropriate cold chain conditions
- the vaccine vial septum has not been submerged in water
- Aseptic technique has been used to withdraw all doses
- The vaccine vial monitor (VVM) (if attached) has not reached the discard point.

7. MARKETING AUTHORISATION HOLDER

Plot No. 1, Biotech Park, Phase-II, Kolthur Village, Shameerpet Mandal, Medchal-Malkajgiri District, Telangana State, INDIA - 500078

Registered Office: Biological E. Limited
18/1&3, Azamabad, Hyderabad – 500020, INDIA.

8. MARKETING AUTHORISATION NUMBER(S)

India: MF/BIO/20/000001

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

28.01.2020 (INDIA)

10. DATE OF REVISION OF THE TEXT

April 2023