SUMMARY OF PRODUCT CHARACTERISTICS

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

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.

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

COMPOSITION

Each dose of 0.5 mL contains:

Typhoid Vi Polysaccharide[1] : 25 µgconjugated to 16.7µg to 100µg of CRM197
Sodium chloride and phosphate buffer: q.s
2-Phenoxyethanol (as Preservative) : 5 mg

[1]Produced from *C. freundii sensu lato* 3056

3. PHARMACEUTICAL FORM

Solution for Intramuscular Injection.

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:

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.

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

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 causedby *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 anaphylacticreactions 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 ofinteraction:

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:

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

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: ≥ 10%

Common: ≥ 1% and < 10%

Uncommon: ≥ 0.1% and < 1%

Rare: ≥ 0.01% and < 0.1%

Very rare: < 0.01%.

<u>Reporting of suspected adverse reactions</u>

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to **TMDA**

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 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.

- **Site and Mechanism of Action**

Evaluation of pharmacokinetic properties is not required for vaccines

- **Clinical Trials**

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 PolysaccharideVaccine 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 andFever.

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 µg/mL and above the long-term protective seroconversion threshold value of ≥ 4.3 µg/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 µg/mL and 96.90%, 95.12% and 94.05% using long-term threshold value of ≥ 4.3 µg/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%.

5.2. Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines

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. Handling of mullti 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 thediscard point.

7. MARKETING AUTHORISATION HOLDER

Plot No. 1, Biotech Park, Phase-II, Kolthur Village,

Shameerpet Mandal,Medchal-Malkajgiri District,

Telangana State,

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Registered Office:

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8. MARKETING AUTHORISATION NUMBER(S)

TAN 22 V 0123

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THEAUTHORISATION

11th April, 2022

10. DATE OF REVISION OF THE TEXT