PUBLIC ASSESSMENT SUMMARY REPORT – Typhoid Vi Conjugate Vaccine (TYPHIBEV), Biological E. Limited, India

What is TYPHIBEV Vaccine?

TYPHIBEV, Typhoid Vi Conjugate Vaccine is a clear, colorless solution, free from visible particulate matter. The vaccine contains 25 µg of Vi Polysaccharide conjugated to 16.7µg – 100µg of CRM_{197} (Typhoid conjugate bulk antigen), Sodium Chloride and Phosphate Buffer which is used as buffering agent and 2-Phenoxyethanol as preservative in vaccine formulation. The polysaccharide is manufactured using *Citrobacter freundii* sensu lato 3056 (Vi) and is conjugated to CRM_{197} as a carrier protein.

Two presentations are available for TYPHIBEV vaccine 0.5 mL (single dose) and 2.5 mL (multi dose - 5 dose) with the following targeted composition per dose:

Name of ingredients	**Unit and/or percentage formula per single human dose - 0.5 mL**
Active ingredients: Typhoid Vi Polysaccharide conjugated to 16.7 µg – 100 µg of CRM_{197}	 25 µg
Excipients: Sodium dihydrogen phosphate dihydrate Disodium hydrogen phosphate anhydrous Sodium Chloride Water for injection 2-Phenoxyethanol (as Preservative)	 0.475 mg 1 mg 2.34 mg q.s. to 0.5 mL 5 mg

The vaccine is supplied in USP Type 1 clear glass vial 3 mL for Single Dose and Multi Dose (2.5 mL - 5 dose), stoppered with 13mm grey bromobutyl rubber stoppers and sealed with 13mm aluminium flip off seals.

Real time and accelerated stability data support the use of a Vaccine Vial Monitor (VVM30).

What is TYPHIBEV Vaccine used for?

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.

How is TYPHIBEV Vaccine used?

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.

Primary vaccination:

The immunizing dose for infants, children, adolescents and adults aged ≥ 6 months to ≤ 45 years is single dose of 0.5 mL. After immunization the vaccine protection will take approximately 2 to 3 weeks to become effective.

Precautions for use:

TYPHIBEV Vaccine should not be injected into the gluteal area or areas where there may be a nerve trunk, neither should it be administered intravenously, intradermally, or subcutaneously.

For multi-dose vials a new syringe should be used each time to vaccinate.

TYPHIBEV, 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. 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.

Typhoid Vi Conjugate Vaccine should not be mixed with other vaccines or medicinal products in the same syringe.

What are the vaccine characteristics of TYPHIBEV Vaccine?

Real time and accelerated stability data support the assigned shelf-life of 24 months at 2°C-8°C with stability data support the use of a Vaccine Vial Monitor (VVM30). Opened vials policy on multi-dose is used in subsequent immunization session for up to a maximum of 28 days provided that all of the following conditions are met (as described in the WHO policy statement:

- Multi-dose vial Policy (MDVP) - Revision 2014 WHO/IVB/14.07.
- The vaccine is currently prequalified by WHO.
- The expiry date of the vaccine has not passed.
- The vaccine is approved for use for up to 28 days after opening the vial, as determined by WHO.
- The vaccine vial has been stored under appropriate cold chain (at +2ºC to +8ºC).
- 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.

An opened vial must be discarded immediately if any of the following conditions applies:

- Sterile procedures have not been fully observed.
- There is even a suspicion that the opened vial has been contaminated, or there is visible evidence of contamination such as change in appearance of floating particles.

The single dose and multi dose vaccine formulation contains 2-Phenoxyethanol 1 % (w/v) as a preservative.

Who is the regulatory authority responsible for its oversight vis a vis WHO?

TYPHIBEV Vaccine received Marketing Authorization in India on 29th January, 2020. The NRA of Record for this vaccine is the Drug Controller General of India under the gamut of Central Drugs Standard Control Organization in India, www.cdsco.nic.in.

How TYPHIBEV Vaccine been studied from the clinical point of view?

The clinical program included two clinical safety and immunogenicity trials. The number of subjects in the phase II study who were exposed to the Biological E. TCV are between ≥6 months to <2 years of age (141), between ≥2 years to <18 years of age (85) and between ≥18 years to <64 years of age (85). An additional 30 adult subjects were exposed to the vaccine in the Phase I study. Thus, a total of only 341 participants received BE-TCV. Data from the following studies were provided:

- Clinical trial "BECT039/TCV-Phase-I/CTP-02" is a phase 1 study to assess the safety, reactogenicity and immunogenicity of BE-TCV conducted in 30 healthy adults from March 2018 to May. 2018 (Clinical trial registry India No. CTRI/2018/03/012558).

- Clinical trial "BECT053/TCV-Phase-IIbyIII/CTP-01" is a single blind randomized controlled. This was a Phase-II/III study to evaluate the immunogenicity and safety of BE-TCV in healthy infants, children and adults in comparison with Typbar TCV® from December 2018 to April 2019 (Clinical trial registry India No. CTRI/2018/11/016419).

The results of the two submitted clinical trials provided evidence that the immunogenicity of BE-TCV is non-inferior to that of the pre-qualified Typbar-TCV vaccine. Immunogenicity data were limited to 42 days after vaccination.

The safety profile of the vaccine was assessed to be satisfactory.
The manufacturer committed to:

1. To provide the report of the safety study (BECT/TCV-Phase-III/057) when ready.
2. To provide the report of the persistent study (BECT059) as soon as it is available.
3. To provide data on co-administration with other vaccines.
4. To conduct a phase IV safety study – provided synopsis
5. To conduct an effectiveness study –provided synopsis

Other information about evaluation of TYPHIBEV Vaccine:

Assessment of the product was based on appropriate Quality and Clinical dossiers review of the submitted Common Technical Document (CTD) dossier, evaluation of the consistency of final product characteristics, site audit of the manufacturing facilities and follow up of implementation of recommendations made by WHO reviewers during the evaluation.

The vaccine meets WHO requirements of WHO TRS 987, Annex 3 published at:

http://www.who.int/biologicals/areas/vaccines/TRS_987_Annex3.pdf?ua=1

This summary was last updated on 25 Aug 2022 and published on date 29 Sep 2022.