1. NAME OF THE MEDICAL PRODUCT

Tripvac

(Diphtheria, Tetanus and Pertussis Vaccine (Adsorbed))

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 General description

Diphtheria, Tetanus and Pertussis Vaccine (Adsorbed) contains purified diphtheria and tetanus toxoids and inactivated whooping cough organisms. The vaccine is adsorbed onto Aluminium Phosphate as adjuvant and thiomersal is used as a preservative. The vaccine has the appearance of a whitish turbid suspension. The vaccine meets the requirements of WHO.

2.2 Qualitative and quantitative composition

Each dose of 0.5 mL contains:

Diphtheria Toxoid	25 Lf (≥ 30 IU)
Tetanus Toxoid	5.5 Lf (≥ 60 IU)*
B. p*ertussis*	16 IOU (≥ 4.0 IU)**
Adsorbed on Aluminium Phosphate ($AlPO_4$)	≥ 1.5 mg
Preservative: Thiomersal	0.01% w/v

*≥ 40 IU when tested in guinea pigs and ≥ 60 IU when tested in mice

** The lower fiducial limit (p=0.95) of the estimated potency is not less than 2.0 IU.

3. PHARMACEUTICAL FORM

Diphtheria, Tetanus and Pertussis Vaccine (Adsorbed) (DTwP) is a whitish turbid suspension for intramuscular injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Diphtheria, Tetanus and Pertussis Vaccine (Adsorbed) (DTwP) is indicated for primary immunization of infants, above the age of six weeks against diphtheria, tetanus and whooping cough diseases. The vaccine can be safely and effectively given at the same time as BCG, Measles, Polio (OPV and IPV), Hepatitis B, Yellow fever, *Haemophilus influenzae* type b vaccines and Vitamin A supplementation.

4.2 Posology and method of administration

For the purpose of primary immunization it is recommended that 3 doses of 0.5 mL of DTwP vaccine should be given intramuscularly at 4-week interval between doses for infants, above the age of six weeks. The vaccine vial should be shaken well to homogenize the suspension. The anterolateral aspect of the upper thigh is the preferred site of injection (An injection into a child's buttocks may cause injury to the sciatic nerve and is not recommended). It must not be injected in to the skin as this may give rise to local reaction. During the course of primary immunization, injection should not be administered more than once at the same time. The first dose should be given at approximately 6 weeks of age. A sterile needle and sterile syringe should be used for each injection. Special care should be taken to ensure that the injection doses not enter a blood vessel.

<u>Immune Deficiency</u>

Individuals infected with Human Immunodeficiency Virus (HIV), both symptomatic and asymptomatic should be immunized with DTwP according to standard immunization schedules.

4.3 Contraindications

Hypersensitivity to any component of the vaccine is a contraindication for the use of vaccine. It is contra-indicated to use this vaccine in persons who developed an immediate anaphylactic reaction to previous dose or to any constituent of the vaccine.

It is a contraindication to administer this vaccine in the presence of any evolving neurological conditions. DTwP should not be given to children with any coagulation disorder, including thrombocytopenia that would contraindicate intramuscular injection.

The vaccine is not recommended for use in individuals 7 years of age and older.

Encephalopathy after a previous dose is a contraindication for further use. Immunization should be postponed if the infant has an acute disease. However, low grade fever, mild respiratory infections should not be considered as contraindications.

4.4 Specials warnings and precautions for use

If any of the following events occur on receipt of DTwP, the decision to give subsequent doses of vaccine should be carefully considered.

1. Temperature ≥ 40°C within 48 hours not due to identifiable causes.
2. Collapse or shock like state (hypotonic-hypo responsive episode) within 48 hours.
3. Persistent, inconsolable crying lasting ≥ 3 hours, occurring within 48 hours.
4. Convulsions with or without fever occurring within 3 days.

Epinephrine injection (1:1000) must be immediately available should an acute anaphylactic reaction occur to any component of the vaccine. All known precautions should be taken to prevent adverse reactions. This includes the review of the patient's history with respect to possible sensitivity and any previous adverse reactions to the vaccine or similar vaccines, previous immunization history and current health status. Immunosuppressed patients may not respond.

Inform the patient or the guardian of the patient, the benefits and risks of immunization. Special care should be taken to ensure that the injection does not enter a blood vessel.

A separate syringe and needle should be used for each child. It is extremely important when the child returns for the next dose in the series, that the parent or guardian of the child should be questioned concerning occurrence of any symptoms and/or signs of adverse reactions after the previous dose.

4.5 Interaction with other medical products and other forms of interaction

As with other intramuscular injections, use with caution in patients on anticoagulant therapy. Immunosuppressive therapies, including irradiations, anti-metabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiological dose), may reduce the immune response to the vaccine. Short term (< 2 weeks) corticosteroids therapy, intra-articular bursa or tendon injections with corticosteroids would not be immunosuppressive.

4.6 Fertility, pregnancy and lactation

Fertility

Not applicable

Pregnancy

Not applicable.

Lactation

Not applicable.

4.7 Effects on the ability to drive and use machines

Not applicable

4.8 Undesirable effects

Mild local or systemic reactions are common. Some temporary swelling, tenderness and redness at the site of injection together with fever occur in a large proportion of cases. Occasionally severe reactions of high fever (with or without chills), irritability and screaming develop within 24 hours of administration of vaccine. Hypotonic-hyporesponsive episodes have been reported. Febrile convulsions have been reported at a rate of one per 12500 doses administered. Administration of acetaminophen at the time and 4-8 hours after vaccination decreases the subsequent incidence of febrile reactions.

The national childhood encephalopathy study in the United Kingdom showed a small increased risk of acute encephalopathy (primary seizures) following DTwP immunization. However subsequent detailed reviews of all available studies by a number of groups, including the United States Institute of Medicine, the Advisory Committee on Immunization Practices, and the Paediatric Association of Australia, Canada, the United Kingdom and the United States, concluded that the data did not demonstrate a causal relationship between DTwP and chronic nervous system dysfunction in children. Thus there is no scientific evidence that these reactions have any permanent consequences for the children[1]

Rarely anaphylactic reaction and death have been reported after receiving preparations containing DTwP. Polyradiculoneuropathies have been reported rarely following administration of a vaccine containing tetanus toxoid, as a possible etiology.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Pertussis, inactivated, whole cell, combinations with toxoids, ATC code: J07AJ51

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Not available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminium phosphate (prepared from $AlCl_3$ and Tri-sodium phosphate dodecahydrate)
Thiomersal
Sodium chloride
Sodium hydroxide
Hydrochloric acid and
Water for injection

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months (stored at 2°C to 8°C)

6.4 Special precautions for storage

The vaccine vial should be stored at a temperature between 2°C to 8°C throughout its use. Do not freeze. Discard if the vaccine has been frozen.

Presentation available with or without vaccine vial monitor.

The vaccine vial monitor…(Optional)

	✓	Inner square lighter than outer circle. **If the expiry date has not been passed, USE the vaccine.**
	✓	At a later time, inner square still lighter than outer circle. **If the expiry date has not been passed, USE the vaccine.**
	×	Discard point, Inner square matches colour of outer circle. **DO NOT use the vaccine.**
	×	Beyond the discard point: Inner square darker than outer ring. **DO NOT use the vaccine.**

Vaccine Vial Monitor (VVM) is part of the label. The colour dot that appears on the label of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.

6.5 Nature and contents of container

DTwP liquid vaccine is available in the following presentations
Single dose vial of 0.5 mL
Ten dose vial of 5 mL

6.6 Special precautions for disposal and other handling

DTwP vaccine is available as a suspension. Upon storage, a white deposit and clear supernatant may be observed. The vaccine should be shaken well in order to obtain a homogenous turbid white suspension and visually inspected for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either of the above being observed, discard the vaccine.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURER

Marketing authorization holder in Thailand

Biogenetech Co., Ltd.
18 Soi Udomsuk 37, Sukhumvit 103 Rd., Bangjak, Prakanong, Bangkok 10260 THAILAND

Tel. 0-2748-9333, Fax 0-2748-9393

Manufacturer

Biological E. Limited

Plot No. 1, S.P. Biotechnology Park, Phase-II,
Kolthur Village, Shameerpet Mandal
Medchal-Malkajgiri District-500078, Telangana, India

Corporate Address
18/1 & 3, Azamabad, Hyderabad, Telangana-500 020, India
Web: www.biologicale.com

8. References

1. In weekly Epidemiological Record, No. 18, 7 May 1999. Page 139.

9. MARKETING AUTHORISATION NUMBER(S)

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10. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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11. DATE OF REVISION OF THE TEXT

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