SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Product Name: Diphtheria, Tetanus, Pertussis (Whole Cell) and *Haemophilus influenzae* type b conjugated Vaccine (Adsorbed) IP

Brand Name : Easyfour-TT®

Strength: One pediatric dose is 0.5 ml

Pharmaceutical Form: Injectable Vaccine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Qualitative and quantitative composition for Easyfour-TT® vaccine is as given in table below:-

Single paediatric dose of 0.5 ml contains:

Component	Quantity
Active Ingredients	
Diphtheria Toxoid	20 Lf (30 IU)
Tetanus Toxoid	7.5 Lf (60 IU)
Inactivated w-*B. pertussis*	12 OU (4 IU)
HIB (PRP-TT) [Purified capsular antigen i.e. Polyribosyl ribitol phosphate (PRP) of *Haemophilus influenza* type b conjugated with carrier protein Tetanus Toxoid	10 mcg
Inactive Ingredients	
Al^{3+} as Aluminium phosphate gel	0.25 mg
Thiomersal	0.025 mg
Physiological saline	q.s.

* PRP-TT- Purified capsular antigen i.e. Polyribosyl ribitol phosphate (PRP) of *Haemophilus influenzae* type b, conjugated with carrier protein Tetanus Toxoid.

SUMMARY OF PRODUCT CHARACTERISTICS

3. PHARMACEUTICAL FORM

The final product has an appearance of a white or almost white material which sediments at the bottom of the container defining two phases: a clear supernatant essentially protein-free composed of physiological saline with the preservative substance dissolved, plus an aluminium phosphate gel with the antigens adsorbed on it. When shaken, a white or almost white suspension is formed, lasting for some minutes, which is the form in which the product is to be administered.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications:

Easyfour-TT® vaccine is indicated for primary active immunization for prevention against Diphtheria, Tetanus, Pertussis and infections caused by *Haemophilus influenzae* type b in infants from 6 weeks onwards. Three primary doses of vaccine must be administered at interval of at least 4 weeks. A booster vaccine dose must be administered at 15-18 months of age.

4.2 Posology and method of administration:

One paediatric dose is of 0.5 ml.

The prefilled syringe or glass vials containing liquid vaccine vial should be shaken before use to homogenize the suspension. The vaccine should be injected intramuscularly. The anterolateral aspect of the upper thigh is the preferred site of injection, or into the deltoid muscles of older children. Vaccine must not be injected intravenously or subcutaneously

4.3 Contraindications:

Known hypersensitivity to any component of the vaccine or a severe reaction to a previous dose of the combination vaccine or any of its constituents is an absolute contraindication to subsequent doses of the combination vaccine or the specific vaccine known to have provoked an adverse reaction. There are few contraindications to the first dose of DTwP, fits or abnormal cerebral signs or other serious neurological abnormality are contraindications to the pertussis component.

4.4 Special warnings and precautions for use:

As with other vaccines, the administration of Easyfour-TT® should be postponed in subject suffering from acute severe febrile illness.

Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and the possible occurrence of undesirable events) and a clinical examination.

If any of the following events occur in temporal relation to be administration of Easyfour-TT® the decision to give subsequent doses of vaccine containing the pertussis component should be carefully considered:

- Temperature of >40.0°C within 48 hours, not due to another identifiable cause.
- Collapse or shock-like state (hypotonic-hypo-responsive episode) within 48 hours.
- Persistent crying lasting >3 hours, occurring within 48 hours.
- Convulsions with or without fever, occurring within 3 days.

A history of febrile convulsions, a family history of convulsions , a family history of SIDS (Sudden infant Death Syndrome) or a family history an adverse event following Easyfour-TT® vaccination do not constitute contra-indications. Easyfour-TT® should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

As with all injectable vaccine, appropriate medical treatment should always be readily available in case of anaphylactic reactions following the administration of the vaccine. For this reason, the vaccines should remain under medical supervision for 30 minutes after vaccination.

Easyfour-TT® should under no circumstances be administered intravenously or subcutaneously.

4.5 Interaction with other medicinal products and other forms of interaction:

Easyfour-TT® can be administered simultaneously at separate sites or in any temporal relationship with other paediatric vaccines if the administration is as per the recommended immunization schedule.

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Individuals infected with the human immuno-deficiency virus (HIV), both asymptomatic and symptomatic, should be immunized with combined vaccine according to standard schedules.

4.6 Pregnancy and lactation:

Not Applicable, as Easyfour-TT® vaccine is not intended for use in adolescent and adult population.

4.7 Effects on ability to drive and use machines:

Not Applicable, as Easyfour-TT® is not intended for use in adult.

4.8 Undesirable effects:

Side Effects do not differ significantly from the DTwP, and Hib vaccine reactions described separately.

For DTwP, mild local or systemic reactions are common. Some temporary swelling, tenderness and redness at the site of injection together with fever occur in large proportion of cases. Occasionally severe reactions of high fever, irritability and screaming develop within 24 hours of administration.

Hib vaccine is very well tolerated. Localized reactions may occur within 24 hours of vaccination, when recipients may experience pain and tenderness at the injection site. These reactions are generally mild and transient. In most cases, they spontaneously resolve within two to three days and further medical attention is not required. Mild systemic reactions, including fever, rarely occur following administration of Hib vaccine. More serious reactions are very rare; a causal relationship between more serious reactions and the vaccine has not been established.

4.9 Overdose:

Not Applicable, as Easyfour-TT® vaccine is to be administered as per the pediatric immunization schedule under the direct supervision of physicians.

SUMMARY OF PRODUCT CHARACTERISTICS

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties:

Diphtheria: Diphtheria is an acute toxin-mediated infectious disease caused by toxigenic strains of *C. diphtheriae*. Protection against disease is due to the development of neutralizing antibodies to the diphtheria toxin; Anti-Diphtheria antibody concentration of 0.1 IU/mL is regarded as protective.

Tetanus: Tetanus is an acute toxin-mediated infectious disease caused by a potent exotoxin released by *C. tetani*. Protection against disease is due to the development of neutralizing antibodies to the tetanus toxin. A serum tetanus antitoxin level of 0.1 IU/mL is considered protective.

Pertussis: Pertussis (whooping cough) is a disease of the respiratory tract caused by *B. pertussis*. The role of the different components produced by *B. pertussis* in either the pathogenesis of, or the immunity to, pertussis is not well understood. There is no well established serological correlate of protection for pertussis.

Haemophilus influenza type b (Hib): Hib is a leading cause of invasive diseases such as meningitis, bacteraemia, epiglottitis and pneumonia in early childhood. Vaccine engendered antibody directed to the polyribosylribitolphosphate (PRP) capsular polysaccharide has been shown to confer a high level of protection. Anti-PRP antibody concentration of 1 µg / ml is considered protective.

Clinical Studies

The safety and efficacy of Easyfour-TT® vaccine has been evaluated in 6, 10, 14 weeks schedule (3 doses given at 4 weeks intervals). The immune responses for all the four components of the vaccine was found to be non-inferior to the licensed control vaccine.

5.2 Pharmacokinetic properties:

Not Applicable.

5.3 Preclinical safety data:

Panacea Biotec manufactured the combination vaccines i.e. Easyfour-TT® (DTwP-Hib) by utilizing the D, T and wP bulk antigens from WHO prequalified supplier P.T. BioFarma, Indonesia and Hib (PRP-TT) bulk conjugate from PanEra Biotec Pvt. Ltd., Lalru.

Three individual components i.e. Diphtheria, tetanus and whole cell pertussis imported from M/s. PT. BioFarma, Indonesia are well established one and proven to be safe, as, same are being used successfully since last many decades in immunization history. Further, these components have been prequalified by WHO after successful review of its quality and safety.

HIb-TT conjugate vaccine did not produce any adverse effect in Balb/c mice and New Zealand White rabbits with single dose and repeated dose administration.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

- Aluminum phosphate gel
- Thiomersal
- Sodium Chloride
- Water for injection

6.2 Incompatibilities:

The vaccine should not be mixed in the vial or syringe with any other vaccine.

6.3 Shelf life:

36 months from the date of manufacturing, when stored at 5°C ± 3°C.

6.4 Special precautions for storage:

Easyfour-TT® vaccine must be stored and transported at 5°C ± 3°C and can be used until the expiry date indicated on the container label. The vaccine must not be frozen.

6.5 Nature and contents of container:

a. **Single dose vial presentation:** The vaccine in single dose, 0.5ml is filled in USP Type 1 glass vial and stoppered with rubber stopper and sealed with flip off aluminium seal.

b. **Prefilled Syringe presentation:** Single dose Pre-filled syringe of USP type 1 glass containing 0.5 ml vaccine stoppered with plunger stopper and supplied along with 25G needle of 1".

7. MARKETING AUTHORIZATION HOLDER

Panacea Biotec Ltd.
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Himachal Pradesh – 173205, India
Tel. : 01795-674036
E-mail : corporate@panaceabiotec.com
Website: https://www.panaceabiotec.com

8. MARKETING AUTHORIZATION NUMBER(S)

License No. : MB/07/632

9. DATE OF FIRST AUTHORIZATION/ RENEWAL OF THE AUTHORIZATION

The details of the manufacturing authorization obtained from Licensing Authority, India for Easyfour-TT® vaccine manufactured at Vaccine Formulation Plant (VFP), Baddi, Himachal Pradesh, India are as mentioned below:

- Date of first authorization: July 26, 2016
- Renewal of the authorization: granted on September 29, 2017 valid up to 28.09.2022
- Retained upto September 28, 2027