For the use of a Registered Medical Practitioner only

1. NAME OF THE MEDICINAL PRODUCT.

Diphtheria and Tetanus Vaccine (Adsorbed) for Adults and Adolescents I.P.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 0.5 mL contains:

Diphtheria Toxoid	≤ 4.5 Lf (NLT 2 IU)
Tetanus Toxoid	≥ 7.5 Lf (NLT 20 IU)
Aluminium [Al^{3+}] as $AlPO_4$ gel	NMT 1.25 mg
2-Phenoxy Ethanol	2.5 mg

3. PHARMACEUTICAL FORM

Suspension for intramuscular injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Diphtheria and Tetanus Vaccine (Adsorbed) for Adults and Adolescents I.P. is indicated for active immunization of children 10 years of age or older, adolescents and adults, against tetanus and diphtheria.

Note:
In order to prevent adverse reactions to the protein of diphtheria toxoid, the quantity of the toxoid has been markedly reduced.

After a primary immunization course of either DTP or Td, adsorbed Td for adults may be used as a booster at intervals of approximately 10 years, but with a minimum of at least one year between doses. It can safely replace monovalent tetanus toxoid (TT) vaccine, including during pregnancy.

No safety and immunogenicity data are available on the concomitant administration of this vaccine with other licensed vaccines.

This vaccine is not to be used for the treatment of tetanus or diphtheria infection.

4.2 Posology and method of administration

Dosage:

The primary schedule of two injections of 0.5 ml at least four weeks apart followed by a third injection 6 to 12 months after the second dose. The vaccine should also be given as a single booster immunization every 5 to 10 years.

Method of administration: -

The vaccine should be injected intramuscularly. The preferred site for injection is deltoid muscle of the upper arm. Care should be taken not to inject into the blood vessel or the skin. Only sterile syringe and needle should be used for each injection. The vaccine should be well shaken before use.

Product which has been exposed to freezing should not be used.

The vaccine should be visually inspected for any foreign particulate matter and / or variation of physical aspect prior to administration. In event of either being observed, discard the vaccine.

Immune deficiency

Individuals infected with human immune deficiency virus (HIV) both asymptomatic and symptomatic, should be immunized with Td Vaccine according to standard schedules. Although the data are limited and further studies are being encouraged, there is no evidence to date of any increased rate of adverse reactions using this vaccine in symptomatic or asymptomatic HIV infected adults and adolescents.

4.3 Contraindications

The vaccine should not be given to persons who showed a severe reaction to a previous dose of Diphtheria and Tetanus vaccine.

A history of systemic allergic or neurologic reactions following a previous dose of Td vaccine is an absolute contraindication for further use.

Immunization should be deferred during the course of an acute illness. Vaccination of persons with severe, febrile illness should generally be deferred until these persons have recovered. However, the presence of minor illnesses such as mild upper respiratory infections with or without fever should not preclude vaccination.

4.4 Special warnings and precautions for use

The possibility of allergic reactions in individuals sensitive to the component of the vaccine should be kept in mind. Adrenaline injection (1:1000) MUST be immediately available should an acute anaphylactic reaction occur to any component of the vaccine. The mainstay in the treatment of severe anaphylaxis is the prompt use of adrenaline, which can be lifesaving. It should be used at the first suspicion of anaphylaxis.

A separate sterile needle and syringe should be used for each individual to prevent transmission of infectious agents. As with the use of all vaccines the vaccinees should remain under observation for not less than 30 minutes for any possibility of occurrence of immediate or early allergic reactions. Hydrocortisone and antihistaminic should also be available in addition to supportive measures such as oxygen inhalation.

Special care should be taken to ensure that the injection does not enter a blood vessel.
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.

As with other vaccines, vaccination with Td vaccine may not protect all individuals.

4.5 Interaction with other medicinal products and other forms of interaction

As with other intramuscular injections, use with caution in patients on anticoagulant therapy. immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses) may reduce the immune response to vaccines.

If Td and Tetanus Immune Globulin (TIG) or Diphtheria Antitoxin are administered concurrently, separate syringes and separate sites should be used.

4.6 Pregnancy and lactation

Pregnancy: Animal reproduction and fertility studies have not been conducted with Td vaccine. It is also not known whether Td vaccine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Td vaccine should be given to a pregnant woman only if clearly needed, as per national recommendations.

Lactation: It is not known whether the active substances included in Td vaccine are excreted in human milk. The effect of administration of Td vaccine during lactation has not been assessed. As Td vaccine is inactivated, any risk to the mother or the infant is improbable. However, the risks and benefits of vaccination should be assessed before making the decision to immunize a nursing woman.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

The safety of Td vaccine of M/s. Zydus Lifesciences Ltd. was established in a phase II/III clinical trial conducted in India. It was a randomized comparative study in which a total of 458 healthy subjects aged 10 to 60 years were enrolled into one of the two study groups; 231 subjects were administered Td vaccine of M/s. Zydus Lifesciences Ltd. and 227

subjects were administered a comparator Td vaccine. The local adverse events (AEs) reported after administration of Td vaccine of M/s. Zydus Lifesciences Ltd. included injection-site pain (16.0%), injection-site swelling (2.6%), injection-site redness (1.7%) and injection-site induration (0.9%). The systemic AEs reported after administration of Td vaccine of M/s. Zydus Lifesciences Ltd. included headache (2.2%), malaise (1.7%), fever (0.9%), myalgia (0.4%) and arthralgia (0.4%). Incidence of AEs reported in the subjects who had received Td vaccine of M/s. Zydus Lifesciences Ltd. was comparable to the incidence of AEs reported in the subjects who had received comparator Td vaccine. No serious adverse event (SAE) was reported in any subject in that clinical trial.

Adverse reactions are generally mild, transient and confined to the site of injection. Occasionally a nodule may develop at the site of injection, but this is rare.

4.9 Overdose

No case of overdose has been reported

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Tetanus: Tetanus is an acute disease caused by an extremely potent neurotoxin produced by *C. tetani*. Protection against disease is due to the development of neutralizing antibodies to tetanus toxin. A tetanus antitoxin level of at least 0.1 IU/mL as measured by the ELISA used in clinical studies of Td vaccine is considered as protective for tetanus. Levels of 1.0 IU/mL have been associated with long-term protection.

Diphtheria: Diphtheria is an acute toxin-mediated disease caused by toxigenic strains of *C. diphtheriae*. Protection against disease is due to the development of neutralizing antibodies to diphtheria toxin. A serum diphtheria antitoxin level of 0.01 IU/mL is the lowest level giving some degree of protection. Antitoxin levels of at least 0.1 IU/mL are generally regarded as protective. A level of at least of 1.0 IU/mL has been associated with long-term protection.

Immune response:

The immunogenicity of Td vaccine of M/s. Zydus Lifesciences Ltd. was evaluated in a phase II/III clinical trial conducted in India. In that study, the proportion of subjects who had who were administered Td vaccine of M/s. Zydus Lifesciences Ltd. and had seroprotective levels of anti-tetanus and anti-diphtheria antibodies (antibody titre ≥ 0.1 IU/ml) at 4 weeks after vaccination was 100.0% and 97.3% respectively. The proportion of subjects who were administered Td vaccine of M/s. Zydus Lifesciences Ltd. and showed booster response to tetanus toxoid and diphtheria toxoid (post-vaccination antibody titre of ≥ 0.4 IU/ml for participants with pre-vaccination antibody titre of <0.1 IU/ml or; four-fold or greater rise in antibody titre post-vaccination for participants with pre-vaccination antibody titre of ≥ 0.1 IU/ml but < 2 IU/ml or; two-fold or greater rise in antibody titre post-vaccination for participants with pre-vaccination antibody titre of ≥ 2 IU/m) at 4 weeks after vaccination was 83.1% and 69.3% respectively. In the subjects who had received Td vaccine of M/s. Zydus Lifesciences Ltd., the pre-vaccination geometric mean titers (GMTs) of anti-tetanus and anti-diphtheria antibodies were 1.42 IU/ml and 0.17 IU/ml respectively, while the post-vaccination GMTs of anti-tetanus and anti-diphtheria antibodies were 9.73 IU/ml and 2.0 IU/ml respectively. A significant rise was reported after vaccination for both anti-tetanus and anti-diphtheria antibody titers.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on single-dose and repeated-dose toxicity studies conducted on Diphtheria and Tetanus Vaccine (Adsorbed).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminium Phosphate gel

2-Phenoxyethanol

6.2 Incompatibilities

This product must not be mixed with other medicinal products.

6.3 Shelf life

The expiry date of the vaccine is indicated on the label and carton of the product.

6.4 Special precautions for storage

The Vaccine should be stored at a temperature between 2 to 8°C. Transportation should also be at 2 to 8°C.

Storage Condition: Store at 2 to 8 °C, Do not Freeze.
Discard Vaccine if frozen, Shake well before use

6.5 Nature and contents of container

Single dose Vial Presentation (0.5ml)

2R Clear Tubular Glass Vial - USP Type I with 13 mm Grey bromo butyl Rubber Stopper and flips off seals.

Multi dose Vial Presentation (5.0ml -10 dose)

5 ml, 20 mm flint tubular Vial - Type I without flat bottom with 20 mm Grey bromo butyl Rubber Stopper and flips off seals.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION

Zydus Lifesciences Limited
Plot Survey No. 23, 25/P, 37, 40/P, 42 to 47, 49 & 50,
Sarkhej - Bavla N. H. 8A, Opp. Ramdev Masala,
Village: Changodar, Taluka: Sanand,
Dist. Ahmedabad – 382 213, State: Gujarat, India.

8. MARKETING AUTHORISATION NUMBER(S)

Permission No. MF/BIO/21/000059

9. DATE OF FIRST AUTHORISATION

15th July, 2021

SmPC updated on: 08.08.2024