PRODUCT MONOGRAPH

# Td ADSORBED

**Tetanus and Diphtheria Toxoids Adsorbed**

Suspension for injection

(For active immunization against Tetanus and Diphtheria)

ATC Code: J07AM51

**Sanofi Pasteur Limited** **Date of Revision:**

Toronto, Ontario, Canada October 2012

# Table of Contents

# Td ADSORBED

**Tetanus and Diphtheria Toxoids Adsorbed**

# PART I: HEALTH PROFESSIONAL INFORMATION

## SUMMARY PRODUCT INFORMATION

### Route of Administration

Intramuscular injection.

### Dosage Form/Strength

Suspension for injection.

Each 0.5 mL dose is formulated to contain:

### Active Ingredients

Tetanus toxoid, diphtheria toxoid

### Clinically Relevant Non-medicinal Ingredients

Excipients: Aluminum phosphate (adjuvant), 2-phenoxyethanol, isotonic solution of sodium chloride in water for injection.

Manufacturing process residuals: formaldehyde is present in trace amounts.

For a complete listing see DOSAGE FORMS, COMPOSITION AND PACKAGING.

## DESCRIPTION

Td ADSORBED [Tetanus and Diphtheria Toxoids Adsorbed], is a sterile, cloudy, white, uniform suspension of tetanus and diphtheria toxoids adsorbed separately on aluminum phosphate and suspended in isotonic sodium chloride solution.

## INDICATIONS AND CLINICAL USE

Td ADSORBED is indicated for active primary and booster immunization for the prevention of tetanus and diphtheria as a single dose in persons 7 years of age and older.

Persons who have had tetanus or diphtheria should still be immunized since these clinical infections do not always confer immunity. (1)

Human Immunodeficiency Virus (HIV)-infected persons, both asymptomatic and symptomatic, should be immunized against tetanus and diphtheria according to standard schedules. (1)

Td ADSORBED is not to be used for the treatment of disease caused by *Corynebacterium diphtheriae* or *Clostridium tetani* infections.

### Pediatrics

Td ADSORBED is not indicated for immunization of children below the age of 7 years.

### Geriatrics

Td ADSORBED is indicated for immunization of persons 7 years of age and older.

### Tetanus Prophylaxis in Wound Management

The need for active immunization with a tetanus toxoid-containing preparation such as Td ADSORBED, with or without passive immunization with Tetanus Immune Globulin, depends on both the condition of the wound and the patient's vaccination history. (1) (See DOSAGE AND ADMINISTRATION.)

## CONTRAINDICATIONS

### Hypersensitivity

Known systemic hypersensitivity reaction to any component of Td ADSORBED or a life-threatening reaction after previous administration of the vaccine or a vaccine containing one or more of the same components are contraindications to vaccination. (1) (2) (3) (See SUMMARY PRODUCT INFORMATION.) Alternatively, such persons may be referred to an allergist for evaluation if further immunizations are considered.

## WARNINGS AND PRECAUTIONS

### General

Before administration of Td ADSORBED, health-care providers should inform the recipient, the parent or guardian of the recipient of the benefits and risks of immunization, inquire about the recent health status of the recipient, review the recipient's history concerning possible hypersensitivity to the vaccine or similar vaccine, previous immunization history, the presence of any contraindications to immunization and comply with any local requirements regarding information to be provided to the recipient/guardian before immunization.

It is extremely important that the recipient, parent or guardian be questioned concerning any signs or symptoms of an adverse reaction after a previous dose of vaccine. (See CONTRAINDICATIONS and ADVERSE REACTIONS.)

The rates and severity of adverse events in recipients of tetanus toxoid are influenced by the number of prior doses and level of pre-existing antitoxins. (3)

As with any vaccine Td ADSORBED may not protect 100% of vaccinated persons.

**Administration Route Related Precautions:** Do not administer Td ADSORBED by intravascular injection; ensure that the needle does not penetrate a blood vessel.

Intradermal or subcutaneous routes of administration are not to be utilized.

Td ADSORBED should not be administered into the buttocks.

**Febrile and Acute Disease:** Vaccination should be postponed in cases of an acute or febrile disease. (2) (3) However, a disease with low-grade fever should not usually be a reason to postpone vaccination.

### Hematologic

Because any intramuscular injection can cause an injection site hematoma in persons with any bleeding disorders, such as hemophilia or thrombocytopenia, or in persons on anticoagulant therapy, intramuscular injections with Td ADSORBED should not be administered to such persons unless the potential benefits outweigh the risks of administration. If the decision is made to administer any product by intramuscular injection to such persons, it should be given with caution, with steps taken to avoid the risk of hematoma formation following injection.

### Immune

The possibility of allergic reactions in persons sensitive to components of the vaccine should be evaluated. Hypersensitivity reactions may occur following the use of Td ADSORBED even in persons with no prior history of hypersensitivity to the product components. (See DOSAGE FORMS, COMPOSITION AND PACKAGING.)

As with all other products, epinephrine hydrochloride solution (1:1,000) and other appropriate agents should be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs. (1) Health-care providers should be familiar with current recommendations for the initial management of anaphylaxis in non-hospital settings, including proper airway management. (1) (4) For instructions on recognition and treatment of anaphylactic reactions, see the current edition of the Canadian Immunization Guide or visit the Health Canada website.

Immunocompromised persons (whether from disease or treatment) may not achieve the expected immune response. If possible, consideration should be given to delaying vaccination until after the completion of any immunosuppressive treatment. Nevertheless, vaccination of persons with chronic immunodeficiency such as HIV infection is recommended even if the immune response might be limited. (1) (2)

### Neurologic

A review by the US Institute of Medicine (IOM) found evidence for a causal relation between tetanus toxoid and both brachial neuritis and Guillain-Barré syndrome (GBS). (5) If GBS occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give Td ADSORBED or any vaccine containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks. (6)

A few cases of demyelinating diseases of the central nervous system, peripheral mononeuropathies and cranial mononeuropathies have been reported following vaccines containing tetanus and/or diphtheria toxoids, although the IOM concluded that the evidence is inadequate to accept or reject a causal relation between these conditions and vaccination. (5)

### Pregnant Women

Animal reproduction and fertility studies have not been conducted with Td ADSORBED. It is also not known whether Td ADSORBED can cause foetal harm when administered to a pregnant

woman or can affect reproduction capacity. Td ADSORBED should be given to a pregnant woman only if clearly needed, as per national recommendations.

### Nursing Women

It is not known whether the active substances included in Td ADSORBED are excreted in human milk. The effect of administration of Td ADSORBED during lactation has not been assessed. As Td ADSORBED 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.

## ADVERSE REACTIONS

### Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect rates observed in practice. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse events that appear to be related to vaccine use and for approximating rates of those events.

During clinical trials, the most common adverse reactions associated with the administration of Td ADSORBED were pain, swelling and redness at the injection site in all age groups and following both primary and booster immunization.

In a clinical study of primary immunization conducted in Canada, Td ADSORBED was administered as a three dose primary series to 18 subjects, 8 of whom were 6 - 9 years of age and 10 of whom were 17 - 56 years of age. In three booster immunization studies conducted in Canada, Td ADSORBED was administered to 773 subjects overall, ranging in age from 12 - 59 years.

In two of the booster immunization studies, one dose of Td ADSORBED was administered to subjects who were presumed to have previously received primary immunization against tetanus and diphtheria, and had not received tetanus or diphtheria toxoid within 5 years prior to enrollment. The results from these studies are presented in Table 1.

No serious adverse events were reported following vaccination with Td ADSORBED in these studies.

**Table 1: Frequencies of Selected Solicited Adverse Events within 72 Hours Following a Dose of Td ADSORBED in Presumably Previously Primed Subjects. (7) (8)**

| Event | TC9704 | | TD9707 |
|---|---|---|---|
| | Adolescents* N = 37 (%) | Adults N = 263 (%) | Adults N = 126 (%) |
| **Injection Site Reactions** | | | |
| **Redness** | 5.4 | 8.4 | 21.4 |
| **Swelling** | 16.2 | 13.3 | 10.3 |
| **Pain** | 81.1 | 84.8 | 84.9 |
| **Systemic Reactions** | | | |
| **Fever** (≥38.0°C) | 2.7 | 4.2 | 0.8 |
| **Chills** | 8.1 | 4.6 | 5.6 |
| **Sore or Swollen Joints** | 8.1 | 5.3 | 5.6 |

* ages 12 – 17 years

### Data from Post-Marketing Experience

The following additional adverse events have been spontaneously reported during the post-marketing use of Td ADSORBED or a similar vaccine manufactured by Sanofi Pasteur, one of identical antigenic content but with thimerosal instead of 2-phenoxyethanol, one of identical tetanus antigen content but lower diphtheria antigen content and thimerosal instead of 2-phenoxyethanol. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure. Decisions to include these events in labelling were based on one or more of the following factors: 1) severity of the event, 2) frequency of reporting, or 3) strength of causal connection to Td ADSORBED.

#### Blood and Lymphatic System Disorders

Lymphadenopathy

#### Immune System Disorders

Allergic reactions including anaphylaxis/anaphylactic reactions, urticaria and oedema of the mouth

#### Nervous System Disorders

Paresthesia, dizziness, syncope

Guillain Barré syndrome (GBS) has been exceptionally reported

**Respiratory, Thoracic and Mediastinal disorders**

Bronchospasm

**Gastrointestinal Disorders**

Vomiting

**Skin and Subcutaneous Tissue Disorders**

Rash, pruritus, rash erythematous, rash maculopapular

**Musculoskeletal, Connective Tissue and Bone Disorders**

Myalgia, pain in extremities

**General Disorders and Administration Site Conditions**

Injection site reactions (including inflammation, mass, oedema, induration, warmth, pruritus, cellulitis, discomfort)

Fatigue, oedema peripheral

Physicians, nurses and pharmacists should report any adverse occurrences temporally related to the administration of the product in accordance with local requirements and to the Global Pharmacovigilance Department, Sanofi Pasteur Limited, 1755 Steeles Avenue West, Toronto, ON, M2R 3T4 Canada. 1-888-621-1146 (phone) or 416-667-2435 (fax).

## DRUG INTERACTIONS

### Vaccine-Drug Interactions

Immunosuppressive treatments may interfere with the development of the expected immune response. (See WARNINGS AND PRECAUTIONS.)

### Concomitant Vaccine Administration

There are no data available on the concomitant administration of Td ADSORBED with other live or inactivated parenteral vaccines. Vaccine administered simultaneously should be given using separate syringes at separate sites, as appropriate for the recipient's age and previous vaccination status. (1)

The vaccine must not be mixed with other medicinal products.

## DOSAGE AND ADMINISTRATION

### Recommended Dose

**Primary Immunization** (1) (9)

For primary immunization of persons 7 years of age and older, a series of three (0.5 mL) doses is required. The first two doses should be given 4 to 8 weeks apart and the third dose 6 to 12 months

later.

Interruption of the recommended schedule with a delay between doses should not interfere with the final immunity achieved with Td ADSORBED. There is no need to start the series over, regardless of the time elapsed between doses.

### Booster Immunization

For booster immunization of persons 7 years of age and older a single (0.5 mL) dose is required. There are currently no data upon which to base a recommendation for the optimal interval for administering subsequent booster doses with Td ADSORBED. For persons who have previously been immunized against tetanus and diphtheria, a dose of 0.5 mL should be administered as a reinforcing dose at approximately 10 year intervals.

Fractional doses (doses <0.5 mL) should not be given. The effect of fractional doses on safety and efficacy has not been determined. (4)

Health-care professionals should refer to the NACI guidelines for tetanus prophylaxis in routine wound management shown in **Table 2**.

**Table 2: NACI Recommended Use of Immunizing Agents in Wound Management** (1)

| History of Tetanus Immunization | Clean, Minor Wounds | | All Other Wounds | |
|---|---|---|---|---|
| | Td* | TIG† (Human) | Td | TIG (Human) |
| Uncertain or <3 doses of an immunization series** | Yes | No | Yes | Yes |
| ≥3 doses received in an immunization series** | No‡ | No | No§ | No†† |

* Adult-type tetanus and diphtheria toxoid.

† Tetanus immune globulin, given at a separate site from the Td.

** Primary immunization is at least 3 doses at age appropriate intervals.

‡ Yes, if >10 years since last booster.

§ Yes, if >5 years since last booster.

†† Yes, if persons are known to have a significant humoral immune deficiency state (eg, HIV, agammaglobulinemia) since immune response to tetanus toxoid may be suboptimal.

A thorough attempt must be made to determine whether a patient has completed primary immunization. Persons who have completed primary immunization against tetanus and who sustain wounds that are minor and uncontaminated should receive a booster dose of a tetanus toxoid-containing preparation if they have not received tetanus toxoid within the preceding 10 years. For tetanus-prone wounds (eg, wounds contaminated with dirt, feces, soil and saliva, puncture wounds, avulsions and wounds resulting from missiles, crushing, burns or frostbite), a booster is appropriate if the patient has not received a tetanus toxoid-containing preparation within the preceding 5 years. (1)

### Administration

Inspect for extraneous particulate matter and/or discolouration before use. (See DESCRIPTION.) If these conditions exist, the product should not be administered.

**Shake the vial well** until a uniform, cloudy, suspension results. Cleanse the vial stopper with a suitable germicide prior to withdrawing the dose. Do not remove either the stopper or the metal seal holding it in place. Aseptic technique must be used. Use a separate sterile needle and syringe, or a sterile disposable unit for each individual recipient, to prevent disease transmission. Needles should not be recapped but should be disposed of according to biohazard waste guidelines. (See WARNINGS AND PRECAUTIONS.)

Before injection, the skin over the site to be injected should be cleansed with a suitable germicide. Administer the total volume of 0.5 mL **intramuscularly** (IM). The preferred site of injection is the deltoid muscle.

Give the patient a permanent personal immunization record. In addition, it is essential that the physician or nurse record the immunization history in the permanent medical record of each patient. This permanent office record should contain the name of the vaccine, date given, dose, manufacturer and lot number.

### Overdosage

For management of suspected drug overdose, contact your regional Poison Control Centre.

## ACTION AND CLINICAL PHARMACOLOGY

### Tetanus and Diphtheria

Tetanus is an acute and often fatal disease caused by an extremely potent neurotoxin produced by *C. tetani*. The toxin causes neuromuscular dysfunction, with rigidity and spasms of skeletal muscles. Protection against disease attributable to *C. tetani* is due to the development of neutralizing antibodies to tetanus toxin. A serum tetanus antitoxin level of at least 0.01 IU/mL, measured by neutralization assay, is considered the minimum protective level. (2) (3) A tetanus antitoxin level of at least 0.1 IU/mL as measured by the ELISA used in clinical studies of Td ADSORBED is considered as protective for tetanus. Levels of 1.0 IU/mL have been associated with long-term protection.

Strains of *C. diphtheriae* that produce diphtheria toxin can cause severe or fatal illness characterized by membranous inflammation of the upper respiratory tract and toxin-induced damage to the myocardium and nervous system. Protection against disease attributable to *C. diphtheriae* 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. (2) (3) Antitoxin levels of at least 0.1 IU/mL are generally regarded as protective. (2) Levels of 1.0 IU/mL have been associated with long-term protection. (3)

## STORAGE AND STABILITY

Store at 2° to 8°C (35° to 46°F). **Do not freeze**. Discard product if exposed to freezing.

Do not use after expiration date.

## DOSAGE FORMS, COMPOSITION AND PACKAGING

### Dosage Forms

Td ADSORBED is supplied as a sterile, cloudy, white, uniform suspension in a vial.

### Composition

Each single dose (0.5 mL) contains:

**Active Ingredients**

| | |
|---|---|
| Tetanus Toxoid | 5 Lf |
| Diphtheria Toxoid | 2 Lf |

**Other Ingredients**

**Excipients**

| | |
|---|---|
| Aluminum Phosphate (adjuvant) | 1.5 mg |
| 2-phenoxyethanol | 0.6% v/v |
| Isotonic solution of Sodium Chloride in Water for Injection | q.s. 0.5 mL |

**Manufacturing Process Residuals**

Formaldehyde is present in trace amounts.

### Packaging

Td ADSORBED is supplied in 0.5 mL single dose glass vials.

The vials are made of Type 1 glass. The container closure system of Td ADSORBED is free of latex (natural rubber).

Td ADSORBED is available in a package of:

5 single dose vials

Vaccine Information Service: 1-888-621-1146 or 416-667-2779. Business hours: 8 a.m. to 5 p.m. Eastern Time, Monday to Friday.

Full product monograph available on request or visit us at www.sanofipasteur.ca

Product information as of October 2012.

Manufactured by:
**Sanofi Pasteur Limited**
Toronto, Ontario, Canada

R15-1012 Canada

# PART II: SCIENTIFIC INFORMATION

## PHARMACEUTICAL INFORMATION

### Drug Substance

Proper name: Tetanus Toxoids and Diphtheria Toxoids,Vaccine Adsorbed

### Product Characteristics

Td ADSORBED [Tetanus and Diphtheria Toxoids Adsorbed] is a sterile, cloudy, white uniform suspension of tetanus and diphtheria toxoids adsorbed separately on aluminum phosphate and suspended in isotonic sodium chloride solution.

*C. diphtheriae* is grown in modified Mueller's growth medium. (10) After purification by ammonium sulphate fractionation, diphtheria toxin is detoxified with formaldehyde and diafiltered. *C. tetani* is grown in modified Mueller-Miller casamino acid medium without beef heart infusion. (11) Tetanus toxin is detoxified with formaldehyde and purified by ammonium sulphate fractionation and diafiltration. Diphtheria and tetanus toxoids are individually adsorbed onto aluminum phosphate.

The adsorbed diphtheria, tetanus components are combined with aluminum phosphate (as adjuvant), 2-phenoxyethanol (as excipient) and water for injection.

When tested in guinea pigs, the tetanus component induces at least 2 neutralizing units/mL of serum and the diphtheria component induces at least 0.5 neutralizing units/mL of serum.

## CLINICAL TRIALS

Three clinical trials (TC9704, TD9707 and Primary Immunization Study), conducted in Canada, provide the clinical basis for the licensure of Td ADSORBED in Canada.

### Study demographics and trial design

**Table 3: Summary of Demographics and Study Design of the Trials with Td ADSORBED**

| Study | Study Design | Dosage and Route of Administration | Study Population* (N = ITT†) | Mean Age (Range) | Gender |
|---|---|---|---|---|---|
| **TC9704** | Randomized, controlled, double-blind, multicentre comparative trial with Td used as control. | 0.5 mL I.M. | Adolescents (N = 37) Adults (N = 263) | 33.5 years (12.0 - 53.9) | Males (N =95) Females (N =(205) |
| **TD9707** | Randomized, controlled, single-blind, multicentre comparative trial with Td used as control. | 0.5 mL I.M. | Adults (N = 126) | 37.93 years (19.43 - 58.48) | Males (N = 44) Females (N = 82) |
| **Primary Immunization study** | Open label, single center trial | 0.5 mL I.M. | Children (N=8) Adults (N=9) | 18.75 years (7 - 30.5) | Males (N=5) Females (N=12) |

* All studies required participants to be in good health and not have been vaccinated against diphtheria, or tetanus within the last 5 years.

† Intent-to-Treat (ITT) population includes all participants who were randomized and received Td ADSORBED.

The efficacy of tetanus toxoid and diphtheria toxoid used in Td ADSORBED [Tetanus and Diphtheria Toxoids Adsorbed] was determined on the basis of immunogenicity studies.

## Immunogenicity

Serological correlates of protection have been defined for diphtheria and tetanus. The efficacy of the tetanus toxoid and diphtheria toxoid used in Td ADSORBED was inferred by the demonstration that the immune responses to these antigens attain levels previously established as protective (≥0.1 IU/mL). (2) (3)

A serum diphtheria antitoxin level of 0.01 IU/mL is the lowest level giving some degree of protection. Antitoxin levels of ≥0.1 IU/mL are generally regarded as protective. Levels of 1.0 IU/mL have been associated with long-term protection. (2)

A serum tetanus antitoxin in level of ≥0.01 IU/mL measured by neutralization assay is considered the minimum protective level. (12) A tetanus antitoxin level ≥0.1 IU/mL as measured by the ELISA used in clinical studies of Td ADSORBED is considered protective. (3)

## Primary Immunization

Primary immunization with tetanus toxoid and diphtheria toxoid used in Td ADSORBED, administered as a series of three doses of Td was evaluated in 17 participants ages 6 to 56 years in a study conducted in Canada. The first two doses were administered two months apart, followed by a third dose six to eight months after the second dose. Serum tetanus antitoxin levels were measured by an in vivo neutralizing assay and serum diphtheria antitoxin levels were measured by an in vitro neutralizing assay. All 17 participants had serum tetanus and diphtheria antitoxin levels pre-vaccination and 7 days post-vaccination <0.01 IU/mL, consistent with no previous immunization. Four weeks following the second dose, all 17 participants had a serum tetanus antitoxin level >0.1 IU/mL and a serum diphtheria antitoxin level ≥0.01 IU/mL. Four weeks following the third dose, all 17 participants had a serum diphtheria antitoxin level >0.1 IU/mL.

## Booster Immunization

In two studies conducted in Canada (TC9704 and TD9707), the immune responses to a dose of Td ADSORBED were evaluated in subjects who were presumed to have previously received primary immunization against tetanus and diphtheria, and had not received tetanus or diphtheria toxoid within 5 years prior to enrollment. Prior to vaccination and 28 - 35 days following vaccination, serum tetanus antitoxin levels were measured by an ELISA that has been shown to correlate with an *in vivo* neutralizing assay, and serum diphtheria antitoxin levels were measured by an *in vitro* neutralizing assay. The results from these studies are presented in Tables 4 and 5.

**Table 4: Tetanus Antitoxin Levels and Booster Response Rates in Presumably Previously Primed Adolescents and Adults Who Received a Dose of Td ADSORBED**

| Study / Age Group | Timing* | Percent of Subjects with Specified Levels of Antitoxin and a Booster Response | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | ≥0.01 IU/mL | | ≥0.1 IU/mL | | ≥1.0 IU/mL | | Booster Response† | |
| | | % | 95% CI | % | 95% CI | % | 95% CI | % | 95% CI |
| **TC9704** | | | | | | | | | |
| **Adolescents‡ (N = 37)** | **Pre-** | 97.3 | (85.8, 99.9) | 89.2 | (74.6, 97.0) | 10.8 | (3.0, 25.4) | - | - |
| | **Post -** | 100 | (90.5, 100) | 100 | (90.5, 100) | 100 | (90.5, 100) | 100 | (90.5, 100) |
| **Adults (N = 263)** | **Pre-** | 98.9 | (96.7, 99.8) | 95.1 | (91.7, 97.3) | 54.4 | (48.1, 60.5) | - | - |
| | **Post-** | 100 | (98.6, 100) | 99.6 | (97.9, 100) | 98.9 | (96.7, 99.8) | 80.6 | (75.3, 85.2) |
| **TD9707** | | | | | | | | | |
| **Adults (N = 122)** | **Pre-** | 99.2 | (95.5, 100) | 92.6 | (86.5, 96.6) | 59.0 | (49.7, 67.8) | - | - |
| | **Post-** | 100 | (97.0, 100) | 100 | (97.0, 100) | 96.7 | (91.8, 99.1) | 81.2 | (73.1, 87.7) |

* Pre: indicates pre-vaccination.
Post: indicates 28 - 35 days post-vaccination.

† Booster response: ≥4-fold increase in post-vaccination antitoxin level relative to pre-vaccination level and post-vaccination level ≥0.1 IU/mL.

‡ Adolescents ages 12 - 17 years.

**Table 5: Diphtheria Antitoxin Levels and Booster Response Rates in Presumably Previously Primed Adolescents and Adults Who Received a Dose of Td ADSORBED**

| Study / Age Group | Timing* | Percent of Subjects with Specified Levels of Antitoxin and a Booster Response | | | | | |
|---|---|---|---|---|---|---|---|
| | | ≥0.01 IU/mL | | ≥0.1 IU/mL | | Booster Response† | |
| | | % | 95% CI | % | 95% CI | % | 95% CI |
| **TC9704** | | | | | | | |
| **Adolescents‡ (N = 37)** | **Pre-** | 89.2 | (74.6, 97.) | 56.8 | (39.5, 72.9) | - | - |
| | **Post -** | 100 | (90.5, 100) | 100 | (90.5, 100) | 100 | (90.5, 100) |
| **Adults (N = 263)** | **Pre-** | 78.7 | (73.3, 83.5) | 38.4 | (32.5, 44.6) | - | - |
| | **Post-** | 98.9 | (96.7, 99.8) | 84.8 | (79.9, 88.9) | 77.6 | (72.0, 82.5) |
| **TD9707** | | | | | | | |
| **Adults (N = 122)** | **Pre-** | 82.8 | (74.9, 89.0) | 35.2 | (26.8, 44.4) | - | - |
| | **Post-** | 98.4 | (94.2, 99.8) | 89.3 | (82.5, 94.2) | 83.6 | (75.8, 89.7) |

* Pre: indicates pre-vaccination.
Post: indicates 28 – 35 days post-vaccination.

† Booster response: ≥4-fold increase in post-vaccination antitoxin level relative to pre-vaccination level and post-vaccination level ≥0.1 IU/mL.

‡ Adolescents ages 12 - 17 years.

## Safety

### Booster Immunization Studies TC9704 and TD9707 (7) (8)

In two of the booster immunization studies conducted in Canada, one dose of Td ADSORBED was administered to participants who were presumed to have previously received primary immunization against tetanus and diphtheria, and had not received tetanus or diphtheria toxoid within 5 years prior to enrollment. In both studies, telephone questionnaires to inquire about adverse events were administered at approximately 24 hours, 72 hours, and 14 days following vaccination. Information on adverse events that occurred after 14 days was collected at a subsequent visit, approximately one-month following vaccination. Some study sites distributed worksheets to participants to assist in recording adverse events, although the use and content of worksheets were not standardized. Frequencies of selected solicited adverse events reported anytime during the first 72 hours following vaccination are presented in Table 6. One participant in Study TD9707 reported swelling of the entire injected upper limb. No serious adverse events were reported following vaccination with TD ADSORBED in these studies.

**Table 6: Frequencies of Selected Solicited Adverse Events Within 72 Hours Following a Dose of Td Adsorbed in Presumably Previously Primed Subjects**

| Event | TC9704 | | TD9707 |
|---|---|---|---|
| | **Adolescents*** *12 to 17 years old* **N = 37** | **Adults** *18 to 54 years old* **N = 263** | **Adults** *19-59 years old* **N = 126** |
| | **%** | **%** | **%** |
| **Local** | | | |
| Redness | | | |
| Any | 5.4 | 8.4 | 21.4 |
| ≥35 mm | 2.7 | 1.5 | 3.2 |
| ≥50 mm | 2.7 | 1.1 | 0.0 |
| ≥100 mm | 0.0 | 0.4 | 0.0 |
| Swelling | | | |
| Any | 16.2 | 13.3 | 10.3 |
| ≥35 mm | 13.5 | 5.7 | 7.1 |
| ≥50 mm | 10.8 | 3.8 | 4.0 |
| ≥100 mm | 2.7 | 1.5 | 0.8 |
| Pain | | | |
| Any | 81.1 | 84.8 | 84.9 |
| Moderate† or worse | 18.9 | 12.2 | 15.1 |
| Severe‡ | 0.0 | 0.4 | 0.8 |
| **Systemic** | | | |
| Fever | | | |
| ≥38.0 ºC | 2.7 | 4.2 | 0.8 |
| ≥38.3ºC | 0.0 | 0.0 | 0.0 |
| Chills | 8.1 | 4.6 | 5.6 |
| Sore or Swollen Joints | 8.1 | 5.3 | 5.6 |

* Ages 12 - 17 years.
† Moderate - interfered with activities, but did not require medical care or absenteeism.
‡ Severe - incapacitating, unable to perform usual activities, required medical care or absenteeism.

No serious adverse events were reported following vaccination with Td ADSORBED in these studies.

Vaccine Information Service: 1-888-621-1146 or 416-667-2779. Business hours: 8 a. m. to 5 p.m. Eastern Time, Monday to Friday.

Full product monograph available on request or visit us at www.sanofipasteur.ca

Product information as of October 2012.

Manufactured by:

**Sanofi Pasteur Limited**

Toronto, Ontario, Canada

R15-1012 Canada

# References List

1 National Advisory Committee on Immunization (NACI). General Guidelines. Recommended Immunization. Diphtheria Toxoid. Tetanus Toxoid. In: Canadian Immunization Guide. 7th ed. Her Majesty the Queen in Right of Canada, represented by the minister of Public Works and Government Services Canada. 2006. p. 73-4, 80-4, 93-146, 166-71, 309-16.

2 Centers for Disease Control and Prevention (CDC). General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2006;55(RR-15):1-48.

3 Plotkin SA, Orenstein WA, OFFIT PA. Diphtheria Toxoid. Tetanus Toxoid. In: Vaccines. 5th ed. Philadelphia. Elsevier Inc. 2008. p. 130-156, 805-840.

4 American Academy of Pediatrics. Pickering LK, editor. 2006 Red Book: Report of the Committee on Infectious Diseases 27th Ed. Elk Grove Village, IL; 2006. p. 36, 64-7.

5 Stratton KR, et al. editors. Adverse events associated with childhood vaccines; evidence bearing on causality. Washington: National Academy Press, 1994. p 67-117.

6 Centers for Disease Control and Prevention (CDC). General recommendations on immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP). MMWR 2002;51(RR-2):1-35.

7 Data on file at Sanofi Pasteur Limited – Clinical Trial TC9704

8 Data on file at Sanofi Pasteur Limited – Clinical Trial TD9707.

9 Centers for Disease Control and Prevention (CDC). Diphtheria, Tetanus and Pertussis: recommendations for Vaccine Use and Other Preventive Measures: Recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1991:40(RR-10):1-28

10 Mueller JH, Miller PA. Variable factors influencing the production of tetanus toxin. J Bacterial 67(3): 1954. p.271-7.

11 Stainer DW. Production of diphtheria toxin. In: Manclark CR, editor. Proceedings of an informal consultation on the World Health Organization requirements for diphtheria, tetanus, pertussis and combined vaccines. United States Public Health Service. Bethesda, MD. DHHS 91-1174. 1991. p. 7-11.

12 Department of Health and Human Services, Food and Drug Administration. Biological products; Bacterial vaccines and toxoids; Implementation of efficacy review; Proposed rule. Federal Register December 13, 1985;50(240):51013.

**IMPORTANT: PLEASE READ**

# PART III: CONSUMER INFORMATION

## Td ADSORBED

### Tetanus and Diphtheria Toxoids Adsorbed

This leaflet is part III of a three-part "Product Monograph" published when Td ADSORBED was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Td ADSORBED. Contact your doctor or pharmacist if you have any questions about the vaccine.

### ABOUT THIS VACCINE

**What the vaccine is used for:**

Td ADSORBED is a vaccine that is used to boost the body's protection against tetanus and diphtheria. This vaccine may be given to persons 7 years of age and older.

The majority of persons who are vaccinated with Td ADSORBED will produce enough antibodies to protect them against these diseases. However, as with all vaccines, 100% protection cannot be guaranteed.

**What it does:**

Td ADSORBED causes your body to produce its own natural protection against tetanus and diphtheria. After you receive the vaccine, your body begins to make substances called antibodies. Antibodies help your body to fight disease. If a vaccinated person comes into contact with one of the germs that cause these diseases, the body is usually ready to destroy it.

**When it should not be used:**

Do not give Td ADSORBED to:

- persons who are known to have a severe allergy to any ingredient in the vaccine or its container, or who have had a severe allergic reaction after receiving a vaccine that contained similar ingredients.

**What the medicinal ingredient is:**

Each 0.5 mL dose of Td ADSORBED contains: tetanus toxoid and diphtheria toxoid.

**What the important non-medicinal ingredients are:**

Aluminum phosphate, 2-phenoxyethanol, isotonic solution of sodium chloride in water for injection. Residual formaldehyde is present in trace amounts.

**What dosage forms it comes in:**

Td ADSORBED is a liquid vaccine that is injected into a muscle. A single dose is 0.5 mL.

### WARNINGS AND PRECAUTIONS

If you or your child has any of the following conditions, talk to your doctor or nurse BEFORE you or your child receives Td ADSORBED:

- **A high fever or serious illness.** Delay the vaccination until the person is better.
- **An allergy to any component of the vaccine or the container.**
- **A serious nervous system adverse event following a previous tetanus vaccination.**
- **Pregnant or nursing mothers**. It is important that you understand the risks and benefits of vaccination. Td ADSORBED should be given to a pregnant woman only if it is clearly needed. Tell the person giving you the injection if you are pregnant or breast-feeding.
- **A weakened immune system.** The vaccine may provide you with a lower level of protection than it does for people with healthy immune systems. If possible, try to postpone the vaccination until after you have completed the treatment that affects your immune system.
- **A bleeding disorder or taking blood-thinning medications.** Tell the person giving you the injection about your condition. The injection must be done carefully to prevent excessive bleeding.

### INTERACTIONS WITH THIS MEDICATION

DO NOT mix Td ADSORBED with other vaccines or medicinal products in the same syringe.

### PROPER USE OF THIS MEDICATION

**Usual Dose:**

For persons aged 7 years and older for prevention of tetanus and diphtheria.

Td ADSORBED may be used for primary and booster vaccination.

The vaccination should be given in the muscle, preferably in the deltoid (shoulder) region.

**Overdose:**

Not applicable for this vaccine.

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

**Missed Dose:**

Not applicable for this vaccine.

## SIDE EFFECTS AND WHAT TO DO ABOUT THEM

A vaccine, like any medicine, may cause serious problems, such as severe allergic reactions. The risk of Td ADSORBED causing serious harm is extremely small. The small risks associated with Td ADSORBED are much less than the risks associated with getting the diseases.

Tell your doctor, nurse or pharmacist as soon as possible if you do not feel well after receiving Td ADSORBED.

Serious side effects are extremely rare.

Some people who receive Td ADSORBED may have mild side effects such as pain, swelling and redness at the injection site. These side effects usually go away within a few days.

This is not a complete list of side effects. For any unexpected effects while taking Td ADSORBED, contact your doctor, nurse or pharmacist.

## HOW TO STORE IT

Store the vaccine in a refrigerator at 2° to 8°C (35° to 46°F). **Do not freeze.** Throw the product away if it has been exposed to freezing.

Do not use after the expiration date.

Keep out of reach of children.

## REPORTING SUSPECTED SIDE EFFECTS

To monitor vaccine safety, the Public Health Agency of Canada collects case reports on adverse events following immunization.

**For Health Care Professionals:**
If a patient experiences an adverse event following immunization, please complete the appropriate Adverse Events following Immunization (AEFI) Form and send it to your local Health Unit in **your province/territory**.

**For the General Public:**
Should you experience an adverse event following immunization, please ask your doctor, nurse, or pharmacist to complete the Adverse Events following Immunization (AEFI) Form.

If you have any questions or have difficulties contacting your local health unit, please contact Vaccine Safety Section at Public Health Agency of Canada:

By toll-free telephone: (1-866-844-0018)

By toll-free fax: (1-866-844-5931)

Email: caefi@phac-aspc.gc.ca

Web: http://www.phac-aspc.gc.ca/im/vs-sv/index-eng.php

By regular mail:
The Public Health Agency of Canada
Vaccine Safety Section
130 Colonnade Road
A/L 6502A
Ottawa, Ontario
K1A 0K9

**NOTE: Should you require information related to the management of the side effect, please contact your health care provider before notifying the Public Health Agency of Canada. The Public Health Agency of Canada does not provide medical advice.**

**MORE INFORMATION**

This document plus the full product monograph, prepared for health professionals can be found at www.sanofipasteur.ca

You may also contact the vaccine producer, Sanofi Pasteur Limited, for more information.
Telephone: 1-888-621-1146 (no charge) or 416-667-2779 (Toronto area).
Business hours: 8 a.m. to 5 p.m. Eastern Time, Monday to Friday.

This leaflet was prepared by Sanofi Pasteur Limited.

Last revised: October 2012

R15-1012 Canada