

AHFS Category 80:08

275 3107598

Tetanus Toxoid For Booster Use Only




(Not recommended for primary immunization)

DESCRIPTION

Tetanus Toxoid, for intramuscular or subcutaneous use, is a sterile solution of toxoid in isotonic sodium chloride solution. The vaccine is clear or slightly turbid in appearance.

Clostridium tetani culture is grown in a peptone-based medium and detoxified with formaldehyde. The detoxified material is then purified by serial ammonium sulfate fractionation, followed by sterile filtration. The toxoid is then diluted with physiological saline solution (0.85%). Each dose contains the preservative thimerosal [(mercury derivative), 25 µg mercury/dose]. This product does not contain an aluminum-containing adjuvant.

Each 0.5 mL dose is formulated to contain 4 Lf (flocculation units) of tetanus toxoid and passes the guinea pig potency test. The residual formaldehyde content, by assay, is less than 0.02%.

CLINICAL PHARMACOLOGY

Tetanus manifests systemic toxicity primarily by neuromuscular dysfunction caused by a potent exotoxin elaborated by *Clostridium tetani*.

Following routine use of tetanus toxoid in the United States (US), the occurrence of tetanus decreased dramatically from 560 reported cases in 1974 to an average of 50-100 cases reported annually from the mid 1970s through the late 1990s. The case-fatality rate has been relatively constant at approximately 30%. During the years 1982-1998, 52% of reported cases were among persons 60 years of age or older. In the mid to late 1990s, the age distribution of reported cases shifted to a younger age group, in part due to an increased number of cases among injection drug users in California. From 1995-1997, persons 20 to 59 years of age accounted for 60% of all cases, with persons 60 years of age or older accounting for only 35%. In the US, tetanus occurs almost exclusively among unvaccinated or inadequately vaccinated persons.¹

In 4% of tetanus cases reported during 1987 and 1988, no wound or other condition was implicated. Non-acute skin lesions, such as ulcers, or medical conditions such as abscesses, were reported in association with 14% of cases.²

Neonatal tetanus occurs among infants born under unhygienic conditions to inadequately vaccinated mothers. Vaccinated mothers confer protection to their infants through transplacental transfer of maternal antibody. From 1972 through 1984, 29 cases of neonatal tetanus were reported in the US.² Since 1984, only three cases of neonatal tetanus have been reported in all infants of unvaccinated or inadequately vaccinated mothers.³

Spores of *C tetani* are ubiquitous. Serologic tests indicate that naturally acquired immunity to tetanus toxin does not occur in the US.² Thus, universal primary vaccination, with subsequent maintenance of adequate antitoxin levels by means of appropriately timed boosters, is necessary to protect all age-groups. Tetanus toxoid is a highly effective antigen, and a completed primary series generally induces protective levels of serum antitoxin that persists for 10 or more years.² In a trial of 26 adults given a booster dose of Tetanus Toxoid, 81% of the subjects demonstrated a 2-fold or greater rise in serum antitoxin antibody levels.⁴ There are no studies of this product used as a primary series.

INDICATIONS AND USAGE

Tetanus Toxoid is indicated for booster injection only for persons 7 years of age or older against tetanus. This vaccine is NOT indicated for primary immunization.

Primary immunization schedule for children under 7 years of age (prior to seventh birthday) should consist of five doses of a vaccine containing tetanus toxoid. The initial three doses are given as Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP) vaccine, administered intramuscularly at intervals of 4 to 8 weeks. A fourth dose of DTaP is recommended at 15 to 20 months of age. The interval between the third and fourth dose should be at least 6 months. A fifth dose of DTaP is given before school entry (kindergarten or elementary school) at 4 to 6 years of age, unless the fourth dose was given after the fourth birthday.^{5,6} In instances where the pertussis vaccine component is contraindicated, Diphtheria and Tetanus Toxoids Adsorbed (For Pediatric Use) (DT) should be used for the remaining doses. For persons 7 years of age and older, Tetanus and Diphtheria Toxoids Adsorbed For Adult Use (Td) is preferred to tetanus toxoid alone.^{2,5}

Tetanus Toxoid is interchangeable with Tetanus Toxoid Adsorbed (contains aluminum adjuvant) as a booster, and would only be preferred if aluminum was to be avoided. Although the rate of seroconversion is essentially equivalent with either form, adsorbed toxoids induce more persistent antitoxin titers.² Tetanus Toxoid would be preferred over diphtheria-containing vaccines if there was a contraindication to the diphtheria component.

For the prevention of neonatal tetanus in unvaccinated pregnant women, see PREGNANCY CATEGORY C section.²

This vaccine is NOT to be used for the treatment of tetanus infection.

As with any vaccine, vaccination with Tetanus Toxoid may not protect 100% of individuals.

If passive immunization is required, Tetanus Immune Globulin (TIG) (Human) should be used (see **DOSAGE AND ADMINISTRATION** section).

CONTRAINDICATIONS

HYPERSENSITIVITY TO ANY COMPONENT OF THE VACCINE, INCLUDING THIMEROSAL, A MERCURY DERIVATIVE, IS A CONTRAINDICATION FOR FURTHER USE OF THIS VACCINE.

It is a contraindication to use this or any other related vaccine after a serious adverse event temporally associated with a previous dose including an anaphylactic reaction.

A history of systemic allergic or neurologic reactions following a previous dose of Tetanus Toxoid is an *absolute contraindication* for further use.^{2,5}

If a contraindication to using tetanus toxoid-containing preparations exists in a person who has not completed a primary immunizing course of tetanus toxoid and other than a clean, minor wound is sustained, *only* passive immunization should be given using TIG (Human).²

Elective immunization should be deferred during the course of any febrile illness or acute infection. A minor afebrile illness such as a mild upper respiratory infection should not preclude immunization.²

Elective immunization procedures should be deferred during an outbreak of poliomyelitis.⁸

It is a contraindication to use this or any other related vaccine after a serious adverse reaction temporally associated with a previous dose, including an anaphylactic reaction.

WARNINGS

Intramuscular injections should be given with great care in patients suffering from thrombocytopenia or other coagulation disorders. In this situation, subcutaneous administration of Tetanus Toxoid may be advisable.

A routine booster should not be given more frequently than every ten years. (This guideline should not preclude wound management considerations.)

Persons who experienced Arthus-type hypersensitivity reactions or temperature greater than 39.4°C (103°F) after a previous dose of a tetanus toxoid-containing preparation usually have very high serum tetanus antibody levels and should not be given even emergency doses of tetanus toxoid-containing preparation more frequently than every 10 years, even if they have a wound that is neither clean nor minor.⁹

Deaths have been reported in temporal association with the administration of Tetanus Toxoid (see **ADVERSE REACTIONS** section).

PRECAUTIONS

GENERAL

Care is to be taken by the health-care provider for the safe and effective use of Tetanus Toxoid.

EPINEPHRINE INJECTION (1:1,000) MUST BE IMMEDIATELY AVAILABLE SHOULD AN ACUTE ANAPHYLACTIC REACTION OCCUR DUE TO ANY COMPONENT OF THE VACCINE.

There is an increased incidence of local and systemic reactions to booster doses of tetanus toxoid when given to previously immunized persons. (Refer to **DOSAGE AND ADMINISTRATION** section for timing of booster injections.) Prior to an injection of any vaccine, all known precautions should be taken to prevent adverse reactions. The physician should have a current knowledge of the literature concerning the use of the vaccine under consideration, including the nature of the adverse reactions that may follow its use. The patient's medical history should be reviewed with respect to possible sensitivity and any previous adverse reactions to the vaccine or similar vaccines, possible sensitivity to dry natural latex rubber, previous immunization history, and current health status (see **CONTRAINDICATIONS** section).

Persons who have a history of Guillain-Barré syndrome (GBS) may be at increased risk of recurrent GBS after subsequent doses of Tetanus Toxoid vaccines. However, in a study in which an estimated 1.2 million doses of tetanus-containing toxoid were administered to persons >18 years of age, two cases of GBS were expected by chance alone during the 6 weeks after vaccination, and only one case was reported. This finding suggests that the risk of GBS after administration of tetanus toxoid is extremely low. The decision to administer tetanus-toxoid-containing vaccine to persons who have had GBS within 6 weeks after receiving tetanus toxoid should be based on the benefits of subsequent vaccination and the risk of the recurrence of GBS.⁹

The expected immune response to Tetanus Toxoid may not be obtained in immunosuppressed patients. Administration of Tetanus Toxoid is not contraindicated in patients with HIV infection.¹⁰

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

Immunosuppressive therapies including radiation, corticosteroids, antimetabolites, alkylating agents, and cytotoxic drugs may reduce the immune response to vaccines. Therefore, routine vaccination should be deferred, if possible, while patients are receiving such therapy.² If Tetanus Toxoid has been administered to persons receiving immunosuppressive therapy, or having an immunodeficiency disorder, an adequate antibody response may not be obtained.⁵ When possible, immunosuppressive treatment should be interrupted when immunization is required due to a tetanus-prone wound.

It is advisable to use DT (For Pediatric Use – 6 years of age and younger) or Td (For Adult Use – 7 years of age and older) in wound prophylaxis instead of tetanus toxoid alone in order to maintain adequate levels of diphtheria immunity.⁵

A separate, sterile syringe and needle or a sterile disposable unit must be used for each patient to prevent transmission of hepatitis or other infectious agents from person to person. Needles should not be recapped and should be properly disposed.

Caution: The stopper of the vial contains dry natural latex rubber, that may cause allergic reactions.

INFORMATION FOR PATIENTS

As part of the child's or adult's immunization record, the date, lot number and manufacturer of the vaccine administered MUST be recorded.¹¹⁻¹³

Patients should be fully informed of the benefits and risks of immunization with Tetanus Toxoid vaccine.

The physician should inform the patients about the potential for adverse reactions that have been temporally associated with Tetanus Toxoid administration. The health-care provider should provide the Vaccine Information Statements (VISs) which are required by the National Childhood Vaccine Injury Act of 1986 to be given with each immunization. Parents or guardians should be instructed to report any adverse reactions to their health-care provider.

IT IS EXTREMELY IMPORTANT WHEN THE CHILD OR ADULT PATIENT RETURNS FOR THE NEXT DOSE IN THE SERIES, THE PARENT, GUARDIAN, OR ADULT PATIENT SHOULD BE QUESTIONED CONCERNING OCCURRENCE OF ANY SYMPTOMS AND/OR SIGNS OF AN ADVERSE REACTION AFTER THE PREVIOUS DOSE (SEE **CONTRAINDICATIONS** AND **ADVERSE REACTIONS** SECTIONS).

The health-care provider should inform the parent, guardian, or adult patient of the importance of completing the immunization series, unless a contraindication to further immunization exists.

The US Department of Health and Human Services has established a Vaccine Adverse Event Reporting System (VAERS) to accept all reports of suspected adverse events after the administration of any vaccine, including but not limited to the reporting of events required by the National Childhood Vaccine Injury Act of 1986.⁵ The toll-free number for VAERS forms and information is 1-800-822-7967.

DRUG INTERACTIONS

If passive immunization for tetanus is needed, TIG (Human) is the product of choice. It provides longer protection than antitoxin of animal origin and causes few adverse reactions. The currently recommended prophylactic dose of TIG (Human) for wounds of average severity is 250 units intramuscularly. When a vaccine containing tetanus toxoid is given at the same time as TIG (Human), separate syringes and separate sites should be used. The ACIP recommends the use of only adsorbed toxoid in this situation.²

The vaccine should be administered subcutaneously in patients on anticoagulant therapy.

Immunosuppressive therapies may reduce the response to vaccines (see **PRECAUTIONS** section).

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY

No studies have been performed to evaluate carcinogenicity, mutagenic potential, or impact on fertility.

PREGNANCY CATEGORY C

Adequate immunization by routine boosters in non-pregnant women of child-bearing age can obviate the need to vaccinate women during pregnancy (see **DOSAGE AND ADMINISTRATION** section).

Animal reproduction studies have not been conducted with Tetanus Toxoid. The risk to the fetus from tetanus toxoid is unknown. The ACIP recommends that an appropriate tetanus toxoid-containing preparation be given to inadequately immunized pregnant women because it affords protection against neonatal tetanus.¹⁰ Waiting until the second trimester is a reasonable precaution to minimize any theoretical teratogenic concern.⁵

It has been reported that Tetanus Toxoid administered to pregnant women prevents neonatal tetanus in newborns.^{14,15} However, the data reported on the safety of Tetanus Toxoid when so used is inconclusive because the incidence of neonatal deaths in New Guinea was significantly higher than in the US. A prospective study in the US has not been done to confirm these reports.¹⁴

NURSING MOTHERS

Tetanus Toxoid does not affect the safety of mothers who are breastfeeding or their infants. Breastfeeding does not adversely affect immune response and is not a contraindication for vaccination.¹⁰

PEDIATRIC USE

SAFETY AND EFFECTIVENESS OF TETANUS TOXOID IN INFANTS BELOW THE AGE OF SIX WEEKS HAS NOT BEEN ESTABLISHED. HOWEVER, THIS VACCINE IS NOT INDICATED FOR CHILDREN UNDER 7 YEARS OF AGE.

GERIATRIC USE

Tetanus Toxoid should only be used in geriatric patients known to have received a primary series (at least 2 doses) of tetanus-containing vaccine, since many such persons have no prior immunity.¹⁶ Clinical studies of Tetanus Toxoid did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

ADVERSE REACTIONS

BODY SYSTEM AS A WHOLE

Adverse reactions may be local and include redness, warmth, edema, induration with or without tenderness as well as urticaria, and rash. Malaise, transient fever, pain, hypotension, nausea and arthralgia may develop in some patients after the injection. Arthus-type hypersensitivity reactions, characterized by severe local reactions (generally starting 2 to 8 hours after an injection) may occur, particularly in persons who have received multiple prior boosters.² On rare occasions, anaphylaxis has been reported following administration of products containing tetanus toxoid. Upon review, a report by the Institute of Medicine (IOM) concluded the evidence established a causal relationship between tetanus toxoid and anaphylaxis.¹⁷ Deaths have been reported in temporal association with the administration of tetanus toxoid-containing vaccines.

NERVOUS SYSTEM

The following neurologic illnesses have been reported as temporally associated with vaccines containing tetanus toxoid: neurological complications^{18,19} including cochlear lesion,²⁰ brachial plexus neuropathies,^{20,21} paralysis of the radial nerve,²² paralysis of the recurrent nerve,²⁰ accommodation paresis, Guillain-Barré syndrome, and EEG disturbances with encephalopathy. The IOM, following review of the reports of neurologic events following vaccination with tetanus toxoid, DT or Td, concluded the evidence favored acceptance of a causal relationship between tetanus toxoid and brachial neuritis and GBS.^{17,23}

Reporting of Adverse Events

The National Vaccine Injury Compensation Program, established by the National Childhood Vaccine Injury Act of 1986, requires physicians and other health-care providers who administer vaccines to maintain permanent vaccination records and to report occurrences of certain adverse events to the US Department of Health and Human Services.¹¹⁻¹³ Reportable events include those listed in the Act for each vaccine and events such as anaphylaxis or anaphylactic shock within 7 days, brachial neuritis within 28 days; any acute complication or sequela (including death) of an illness,⁵ disability, injury, or condition referred to above, or any events that would contraindicate further doses of vaccine, according to this Tetanus Toxoid for Booster Use Only package insert.

Adverse events following immunization with vaccine should be reported by health-care providers to the US Department of Health and Human Services (DHHS) Vaccine Adverse Event Reporting System (VAERS). Reporting forms and information about reporting requirements or completion of the form can be obtained from VAERS through a toll-free number 1-800-822-7967.¹¹⁻¹³

Health-care providers also should report these events to the Pharmacovigilance Department, Sanofi Pasteur Inc., Discovery Drive, Swiftwater, PA 18370 or call 1-800-822-2463.

DOSAGE AND ADMINISTRATION^{2,5}

Parenteral drug products should be inspected visually for extraneous particulate matter and/or discoloration prior to administration whenever solution and container permit. The vaccine should not be used if particulate matter or discoloration is found.

FOR BOOSTER USE ONLY – NOT RECOMMENDED FOR PRIMARY IMMUNIZATION

SHAKE VIAL WELL before withdrawing each dose.

Inject intramuscularly or subcutaneously in the area of the vastus lateralis (lateral mid-thigh) or deltoid. The vaccine should not be injected into the gluteal area or areas where there may be a major nerve trunk.

A needle length \geq one inch is preferred for these age groups because needles less than one inch might be of insufficient length to penetrate muscle tissue in certain adults and older children.¹⁰

Before injection, the skin over the site to be injected should be cleansed with a suitable germicide. After insertion of the needle, aspirate to ensure that the needle has not entered a blood vessel.

After the initial immunization series is completed (see **INDICATIONS AND USAGE** section), a booster dose of 0.5 mL of Tetanus Toxoid should be given intramuscularly every 10 years to maintain adequate immunity. This 10-year period is determined from the last dose administered irrespective of whether it was given earlier in routine childhood immunization or as part of wound management.⁵

Booster Injection After Injury:

A thorough attempt must be made to determine whether a patient has completed primary immunization. Patients with unknown or uncertain previous immunization histories should be considered to have no previous tetanus toxoid doses. Persons who had military service since 1941 can be considered to have received at least one dose. Although most people in the military since 1941 may have completed a primary series of tetanus toxoid, this cannot be assumed for each individual. Patients who have not completed a primary series may require tetanus toxoid and passive immunization (TIG – Human) at the time of wound cleaning and debridement (**TABLE 1**).²

Available evidence indicates that complete primary vaccination with tetanus toxoid provides long-lasting protection \geq 10 years for most recipients. Consequently, after complete primary tetanus vaccination, boosters, even for wound management, need to be given only every 10 years when wounds are minor and uncontaminated. For other wounds, a booster is appropriate if the patient has not received tetanus toxoid within the preceding five years. Persons who have received at least two doses of tetanus toxoid rapidly develop antitoxin antibodies.²

Tetanus and Diphtheria Toxoids Adsorbed for Adult Use (Td) is the preferred vaccine for active tetanus immunization in wound management of patients \geq 7 years of age. Because a large proportion of adults are susceptible to diphtheria, this vaccine enhances diphtheria protection. Thus, by taking advantage of acute health-care visits, such as for wound management, some patients can be protected who otherwise would remain susceptible. For inadequately vaccinated patients of all ages, completion of primary vaccination at the time of discharge or at follow-up visits should be ensured.²

Tetanus Toxoid is interchangeable with Tetanus Toxoid Adsorbed (contains aluminum adjuvant) as a booster, and would only be preferred if aluminum was to be avoided. Tetanus Toxoid would be preferred over diphtheria-containing vaccines if there was a contraindication to the diphtheria component.

TABLE 1^{2,5} Summary Guide to Tetanus Prophylaxis in Routine Wound Management*

History of Adsorbed Tetanus Toxoid (Doses)	Clean, Minor Wounds		All Other Wounds**	
	Td	TIG	Td	TIG
Unknown or < three	Yes	No	Yes	Yes
≥Three	No†	No	No§	No

* Important details are in the text of the insert.

** Such as, but not limited to, wounds contaminated with dirt, feces, soil, and saliva; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns, and frostbite.

† Yes, if >10 years since last dose.

§ Yes, if >5 years since last dose. (More frequent boosters are not needed and can accentuate side effects.)

If passive immunization for tetanus is needed, TIG (Human) is the product of choice. It provides longer protection than antitoxin of animal origin and causes few adverse reactions. The currently recommended prophylactic dose of TIG (Human) for wounds of average severity is 250 units intramuscularly. When tetanus toxoid and TIG (Human) are given concurrently, separate syringes and separate sites should be used. TIG should not be given with Tetanus Toxoid, but only with Tetanus Toxoid Adsorbed.²

HOW SUPPLIED

Vial, 15 Doses (7.5 mL) – Product No. 49281-812-84

CPT® Code: 90749

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STORAGE

Store at 2° to 8°C (35° to 46°F). DO NOT FREEZE.

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Manufactured by:
Sanofi Pasteur Inc.
 Swiftwater PA 18370 USA

Product information
 as of December 2005

sanofi pasteur