

A.H.F.S. Category 80:08

Tetanus Toxoid USP For Booster Use Only

(Not recommended for primary immunization)



Caution: Federal (USA) law prohibits dispensing without prescription.

DESCRIPTION

Tetanus Toxoid USP, 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%) and thimerosal (a mercury derivative) is added to a final concentration of 1:10,000.

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 is an intoxication manifested primarily by neuromuscular dysfunction caused by a potent exotoxin elaborated by *Clostridium tetani*.

The occurrence of tetanus in the United States has decreased dramatically from 560 reported cases in 1947 to a record low of 48 reported cases in 1987. Tetanus in the United States is primarily a disease of older adults. Of 99 tetanus patients with complete information reported to the Centers for Disease Control and Prevention (CDC) during 1987 and 1988, 68% were ≥ 50 years of age, while only six were < 20 years of age. Overall, the case-fatality rate was 21%.¹ In 1992, 45 cases were reported of which 82% were ≥ 50 years of age.² The disease continues to occur almost exclusively among persons who are unvaccinated or inadequately vaccinated or whose vaccination histories are unknown or uncertain.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.¹

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 United States. No cases of neonatal tetanus were reported in the period 1985 to 1989.¹

Spores of *C. tetani* are ubiquitous. Serologic tests indicate that naturally acquired immunity to tetanus toxin does not occur in the United States.¹ Thus, universal primary vaccination, with subsequent maintenance of adequate antitoxin levels by means of appropriately timed boosters, is necessary to protect persons among all age-groups. Tetanus toxoid is a highly effective antigen, and a completed primary series generally induces protective levels of neutralizing antibodies to tetanus toxin that persist for ≥ 10 years.¹

INDICATIONS AND USAGE

Tetanus Toxoid USP 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 should consist of five doses of a vaccine containing tetanus toxoid. The initial three doses are given as Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (DTP) vaccine, administered intramuscularly at 2-month intervals beginning at 2 months of age. A fourth dose, either of Diphtheria and Tetanus Toxoids and Acellular Pertussis (DTaP) or DTP, is recommended 6 to 12 months after the third dose, usually at 15 to 18 months of age; if given before 15 months. A fifth dose of DTaP or DTP 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. If the pertussis component is contraindicated, Diphtheria and Tetanus Toxoids Adsorbed (For Pediatric Use) (DT) is recommended. For persons 7 years of age and older, Tetanus and Diphtheria Toxoids Adsorbed USP For Adult Use (Td) is preferred to tetanus toxoid alone.^{3,4}

For the prevention of neonatal tetanus in unvaccinated pregnant women, see PREGNANCY section.¹

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

Tetanus toxoid is also available in adsorbed form. Although the rate of seroconversion is essentially equivalent with either form, adsorbed toxoids induce more persistent antitoxin titers.¹

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

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

CONTRAINDICATIONS

A history of systemic allergic or neurologic reactions following a previous dose of Tetanus Toxoid is an absolute contraindication for further use.^{1,3}

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).¹

IT IS ALSO A CONTRAINDICATION TO ADMINISTER TETANUS TOXOID USP TO INDIVIDUALS KNOWN TO BE SENSITIVE TO THIMEROSAL.

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.¹

Elective immunization procedures should be deferred during an outbreak of poliomyelitis.⁵

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

This product contains dry natural latex rubber as follows: The stopper to the vial contains dry natural latex rubber.

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.)

PRECAUTIONS

GENERAL

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

Epinephrine Injection (1:1000) 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. This should include a review of the patient's history with respect to possible sensitivity and any previous adverse reactions (see **CONTRAINDICATIONS** section) to the vaccine or similar vaccines and to possible sensitivity to dry natural latex rubber, and a current knowledge of the literature concerning the use of the vaccine under consideration.

Prior to administration of Tetanus Toxoid USP, health-care personnel should inform the parent, guardian, or adult patient of the benefits and risks of immunization, and also inquire about the recent health status of the patient to be injected.

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.¹ If Tetanus Toxoid USP has been administered to persons receiving immunosuppressive therapy, or having an immunodeficiency disorder, an adequate antibody response may not be obtained.³ When possible, immunosuppressive treatment should be interrupted when immunization is required due to a tetanus-prone wound.

Administration of Tetanus Toxoid USP is not contraindicated in individuals with HIV infection.⁶

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.²

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.

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.^{7,8,9}

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; ADVERSE REACTIONS** SECTIONS).

The health-care provider should inform the parent, guardian, or adult patient of the importance of completing the immunization series.

The health-care provider should provide the Vaccine Information Materials (VIMs) which are required to be given with each immunization.

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 1986.⁷ The toll-free number for VAERS forms and information is 1-800-822-7967.

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. Reportable events include those listed in the Act for each vaccine and events specified in the package insert as contraindications to further doses of the vaccine.^{8,9}

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!

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**REPRODUCTIVE STUDIES – 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 USP. It is also not known whether Tetanus Toxoid USP can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Tetanus Toxoid USP should be given to a pregnant woman only if clearly needed.

Physicians generally avoid prescribing unnecessary drugs and biologics for pregnant women.

However, the ACIP recommends the following: *a previously unvaccinated pregnant woman whose child might be born under unhygienic circumstances (without sterile technique) should receive two doses of Td 4 to 8 weeks apart before delivery, preferably during the last two trimesters. Pregnant women in similar circumstances who have not had a complete vaccination series should complete the three-dose series. Those vaccinated more than 10 years previously should have a booster dose. No evidence exists to indicate that tetanus and diphtheria toxoids administered during pregnancy are teratogenic.*¹

It has been reported that Tetanus Toxoid administered to pregnant women prevents neonatal tetanus in newborns.^{10,11} 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 United States. A prospective study in the United States has not been done to confirm these reports.¹⁰

PEDIATRIC USE

SAFETY AND EFFECTIVENESS OF TETANUS TOXOID USP 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.

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.¹ 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.¹² 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^{13,14} including cochlear lesion,¹⁵ brachial plexus neuropathies,^{15,16} paralysis of the radial nerve,¹⁷ paralysis of the recurrent nerve,¹⁵ 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 Guillain-Barré syndrome.^{12,18}

Reporting of Adverse Events

Reporting by parents or guardians of all adverse events after vaccine administration should be encouraged. 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.^{7,8,9}

Health-care providers also should report these events to the Director of Scientific and Medical Affairs, Aventis Pasteur Inc., Discovery Drive, Swiftwater, PA 18370 or call 1-800-822-2463.

DOSAGE AND ADMINISTRATION^{1,3}

Parenteral drug products should be inspected visually for extraneous particulate matter and/or discoloration prior to administration whenever solution and container permit. If these conditions exist, the vaccine should not be administered.

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.

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.³

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 injections. 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)¹.

Available evidence indicates that complete primary vaccination with tetanus toxoid provides long-lasting protection ≥ 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 develop antitoxin antibodies.

Tetanus and Diphtheria Toxoids Adsorbed for Adult Use USP (Td) is the preferred vaccine for active tetanus immunization in wound management of patients ≥ 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.¹

TABLE 1^{1,3} 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
\geq 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. The ACIP recommends the use of only adsorbed toxoid in this situation.¹

HOW SUPPLIED

Vial, 7.5 mL – Product No. 49281-812-84

STORAGE

Store between 2° – 8°C (35° – 46°F). DO NOT FREEZE.

REFERENCES

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