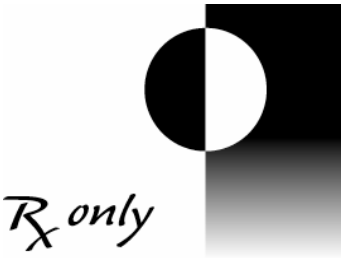
AHFS Category 80:08

Tetanus Toxoid Adsorbed



DESCRIPTION

Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc., for intramuscular injection, is a sterile suspension of alum-precipitated (aluminum potassium sulfate) toxoid in an isotonic sodium chloride solution. The vaccine, after shaking, is a turbid liquid, whitish-gray in color.

Clostridium tetani culture is grown in a peptone-based medium containing an extract of bovine muscle tissue and detoxified with formaldehyde. The bovine muscle tissue used in this medium is US sourced. The detoxified material is then purified by serial ammonium sulfate fractionation and diafiltration, followed by sterile filtration. The toxoid is adsorbed to aluminum potassium sulfate (alum). The adsorbed toxoid is diluted with physiological saline solution (0.85%). Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. is supplied in a unit dose 0.5 mL vial, which contains a trace amount of thimerosal [(mercury derivative), (≤ 0.3 μg mercury/dose)] from the manufacturing process. Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. is also supplied in a 5 mL vial, which contains the preservative thimerosal [(mercury derivative), (25 μg mercury/dose)].

Each 0.5 mL dose is formulated to contain 5 Lf (flocculation units) of tetanus toxoid and not more than 0.25 mg of aluminum. The residual formaldehyde content, by assay, is less than 0.02%. The tetanus toxoid induces at least 2 units of antitoxin per mL in the guinea pig potency test.

CLINICAL PHARMACOLOGY

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

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.

Spores of *C tetani* are ubiquitous. Serologic tests indicate that naturally acquired immunity to tetanus toxin does not occur in the US.[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. Following adequate immunization with tetanus toxoid, it is thought that protection persists for at least 10 years. Protection against disease 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 assays, is considered the minimum protective level.[2] More recently, a level of ≥0.1 to 0.2 IU/mL has been considered as protective.[3]

The efficacy of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. was determined on the basis of an immunogenicity study with a comparison to a serological correlate of protection (0.01 antitoxin units/mL) established by the Panel on Review of Bacterial Vaccines & Toxoids.[2]

A Tetanus and Diphtheria Toxoids Adsorbed For Adult Use vaccine manufactured by Aventis Pasteur Inc. was administered to a previously unimmunized rural population 6 to 58 years of age. Among 46 persons with serologic evidence for no pre-existing immunity to tetanus, all had titers of 0.01 AU (antitoxin untis) or more one month after the second and third immunizations.

No immunogenicity data are available on concomitant administration of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. with other US licensed vaccines.

INDICATIONS AND USAGE

Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. is indicated for active immunization of children 7 years of age or older, and adults, for prevention of tetanus.

For immunization of infants and children younger than 7 years of age against tetanus and diphtheria, refer to the manufacturers' package inserts for Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP) and for Diphtheria and Tetanus Toxoids Adsorbed (For Pediatric Use) (DT).

Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. is not to be used for the treatment of active tetanus disease. For use of this vaccine for tetanus prophylaxis in wound management, refer to **DOSAGE AND ADMINISTRATION**.

Persons who have had tetanus should still be immunized since this clinical infection does not always confer immunity.

As with any vaccine, vaccination with Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. may not protect 100% of individuals.

If passive protection against tetanus is required, Tetanus Immune Globulin (Human) (TIG) should be used (see **DOSAGE AND ADMINISTRATION**, TETANUS PROPHYLAXIS IN WOUND MANAGEMENT).

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine, including thimerosal, a mercury derivative, is a contraindication to receipt of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. (See **DESCRIPTION** section).

It is a contraindication to use this vaccine after anaphylaxis or other serious allergic reaction following a previous dose of this vaccine, any other tetanus toxoid-containing vaccine, or any component of this

vaccine. Because of uncertainty as to which component of the vaccine may be responsible, no further vaccination with a tetanus component should be carried out. Alternatively, such individuals may be referred to an allergist for evaluation if further immunizations are to be considered.

WARNINGS

The stopper of the multi-dose vial contains dry natural latex rubber, which may cause allergic reactions in latex-sensitive individuals.

Except under circumstances of wound management (see **DOSAGE AND ADMINISTRATION**), booster doses of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. should not be administered more frequently than as recommended for Td vaccines (ie, at 11-12 years of age if at least 5 years have elapsed since the last dose of tetanus and diphtheria-toxoid containing vaccine, and every 10 years thereafter).[4] More frequent booster doses may be associated with increased incidence and severity of adverse reactions.[1]

Persons who experienced severe Arthus-type hypersensitivity reactions following a prior dose of tetanus toxoid usually have very high serum tetanus antitoxin levels and should not be given even emergency doses of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. more frequently than every 10 years, even if they have a wound that is neither clean nor minor.[5]

Because intramuscular injection can cause injection site hematoma, Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. should not be given to persons with any bleeding disorder, such as hemophilia or thrombocytopenia, or to persons on anticoagulant therapy unless the potential benefits clearly outweigh the risk of administration. If the decision is made to administer Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. in such persons, it should be given with caution, with steps taken to avoid the risk of hematoma formation following injection.

If Guillain-Barré Syndrome occurs within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give subsequent doses of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. or any vaccine containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks.[3]

The Advisory Committee on Immunization Practices (ACIP) has published guidelines for vaccination of persons with recent or acute illness.[3]

PRECAUTIONS

GENERAL

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

EPINEPHRINE INJECTION (1:1000) AND OTHER APPROPRIATE AGENTS AND EQUIPMENT MUST BE IMMEDIATELY AVAILABLE SHOULD AN ACUTE ANAPHYLACTIC REACTION OCCUR DUE TO ANY COMPONENT OF THE VACCINE.

Prior to administration of any dose of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc., the vaccine recipient's current health status and personal health history should be reviewed. This should include a review of the patient's immunization history, any adverse events after previous immunizations and history concerning possible sensitivity to the vaccine and to dry natural latex rubber (contained in the stopper of the multidose vial only), in order to determine the existence of any contraindications to administration of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. and to allow an assessment of the benefits and risks of vaccination.

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

Immunocompromised persons (whether from disease or treatment) may not obtain the expected immune response to Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc.

Administration of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. is not contraindicated in immunocompromised persons.[3,6]

A separate, sterile syringe and needle or a sterile disposable unit should be used for each patient to prevent transmission of blood borne infectious agents. Needles should not be recapped and should be disposed of according to biohazard waste guidelines.

INFORMATION FOR PATIENTS

Prior to administration of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc., health-care providers should inform the parent, guardian, or adult patient of the benefits and risks of immunization.

The health-care provider should inform the parent, guardian, or adult patient about the potential for adverse reactions that have been temporally associated with the administration of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. or other vaccines containing similar components. The parent, guardian or adult patient should be instructed to report any serious adverse reactions to their health-care provider. Adverse events following immunization should be reported by health-care providers to the Vaccine Adverse Event Reporting System (VAERS) (See **ADVERSE REACTIONS**, REPORTING OF ADVERSE EVENTS).

As part of the child's or adult's permanent immunization record, the date, lot number and manufacturer of the vaccine administered MUST be recorded.[7,8,9]

The health-care provider should inform the parent, guardian, or adult patient of the importance of completing the primary immunization series or receiving recommended booster doses, as appropriate.

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.

DRUG INTERACTIONS

For information on concomitant administration of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. with TIG (Human) see **DOSAGE AND ADMINISTRATION,** TETANUS PROPHYLAXIS IN WOUND MANAGEMENT.

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

No information is available regarding concomitant administration of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. with other US licensed vaccines.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY

No studies have been performed with Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. to evaluate carcinogenicity, mutagenic potential, or impact on fertility.

PREGNANCY CATEGORY C

Animal reproduction studies have not been conducted with Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. It is also not known whether Tetanus Toxoid Adsorbed manufactured by Aventis

Pasteur Inc. can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. should be given to a pregnant woman only if clearly needed.

The ACIP has published recommendations for immunizing pregnant women against tetanus.[3]

NURSING MOTHERS

It is not known whether Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. is administered to a nursing woman.

PEDIATRIC USE

Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. is not indicated for infants and children younger than 7 years of age. For immunization of infants and children younger than 7 years of age against tetanus, refer to the manufacturers' package inserts for Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP) and for Diphtheria and Tetanus Toxoids Adsorbed (For Pediatric Use) (DT).

GERIATRIC USE

The clinical study of Tetanus and Diphtheria Toxoids Adsorbed For Adult Use manufactured by Aventis Pasteur Inc. did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

ADVERSE REACTIONS

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 booster doses of a tetanus toxoid containing vaccine.[5]

Cases of allergic or anaphylactic reaction (ie, hives, swelling of the mouth, difficulty breathing, hypotension, or shock) have been reported after receiving some preparations containing tetanus toxoid. Death following vaccine-caused anaphylaxis has been reported.[10]

Certain neurological conditions have been reported in temporal association with some tetanus toxoid-containing vaccines. A review by the Institute of Medicine (IOM) concluded that the evidence favors acceptance of a causal relation between tetanus toxoid and both brachial neuritis and Guillian-Barré syndrome.[10] Other neurological conditions that have been reported include: demyelinating diseases of the central nervous system, peripheral mononeuropathies, cranial mononeuropathies, and EEG disturbances

with encephalopathy (with or without permanent intellectual and/or motor function impairment). The IOM has concluded that the evidence is inadequate to accept or reject a causal relation between these conditions and vaccine containing tetanus toxoid.[10] In the differential diagnosis of polyradiculoneuropathies following administration of a vaccine containing tetanus toxoid, tetanus toxoid should be considered as a possible etiology.[10]

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 of the manufacturer and lot number of the vaccine administered in the vaccine recipient's permanent medical record, along with the date of administration of the vaccine, and the name, address, and title of the person administering the vaccine. The Act further requires the health-care professional to report to the US Department of Health and Human Services (DHHS) the occurrence following immunization of any event set forth in the Vaccine Injury Table that occurs within the time period specified or within 7 days, if that is longer, and any contraindicating event listed in the manufacturer's package insert. For tetanus toxoid, these include anaphylaxis or anaphylactic shock within 7 days; brachial neuritis within 28 days; an acute complication or sequelae (including death) of an illness, disability, injury, or condition referred to above; or any events that would contraindicate further doses of vaccine, according to this package insert for Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc.[8,9]

Reporting by parents, guardians, or adult patients of all adverse events after vaccine administration should be encouraged. Adverse events following immunization should be reported by health-care providers to the 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 Pharmacovigilance Department, Aventis Pasteur Inc., Discovery Drive, Swiftwater, PA 18370 or call 1-800-822-2463.

DOSAGE AND ADMINISTRATION

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

SHAKE VIAL WELL before withdrawing each dose. Discard vial if vaccine cannot be resuspended.

Before injection, the skin over the site to be injected should be cleansed with a suitable germicide.

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

Primary Immunization:

For persons 7 years of age and older who have not been immunized previously against tetanus, the primary immunization series of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. consists of three 0.5 mL doses. The intervals between doses recommended by the ACIP are 4 to 8 weeks between the first and second dose, and 6 to 12 months between the second and third dose.[1]

Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. may be used to complete the primary immunization series for tetanus in children 7 years of age or older who have received one or two doses of whole-cell pertussis DTP, DTaP, and/or DT vaccine. However the safety and efficacy of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. in such children have not been evaluated.

Interruption of the recommended schedule with a delay between doses should not interfere with the final immunity achieved with Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc.. There is no need to start the series over again, regardless of the time elapsed between doses.

Routine Booster Immunization:

Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. is approved for booster immunization in persons 7 years of age and older who have completed primary immunization against tetanus.

Booster immunization against tetanus is recommended by the ACIP in persons 11-12 years of age if at least 5 years have elapsed since the last dose of a tetanus and diphtheria toxoid-containing vaccine.[4] Subsequent routine booster immunization against tetanus is recommended every 10 years. [4,11] If a dose

of a tetanus-toxoid containing vaccine is given sooner than 10 years, as part of wound management or on exposure to diphtheria, the next booster is not needed for 10 years thereafter.[1] MORE FREQUENT BOOSTER IMMUNIZATION AGAINST TETANUS IS NOT RECOMMENDED AND MAY BE ASSOCIATED WITH INCREASED INCIDENCE AND SEVERITY OF ADVERSE REACTIONS.[1,3] (See **WARNINGS** section).

TETANUS PROPHYLAXIS IN WOUND MANAGEMENT

The need for active immunization with a tetanus toxoid-containing preparation, with or without passive immunization with TIG (Human) depends on both the condition of the wound and the patient's vaccination history (Table 1).

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 which are minor and uncontaminated, should receive a booster dose of a tetanus toxoid-containing preparation only 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, and frostbite), a booster is appropriate if the patient has not received a tetanus toxoid-containing preparation within the preceding 5 years. If a booster dose is given sooner than 10 years as part of wound management, the next routine booster should not be given for 10 years thereafter.[1]

Persons who have not completed primary immunization against tetanus, or whose immunization history is unknown or uncertain, should be immunized with a tetanus toxoid-containing product. Completion of primary immunization thereafter should be ensured. In addition, if these persons have sustained a tetanus-prone wound, the use of TIG (Human) is recommended. TIG (Human) should be administered at a separate site, with a separate needle and syringe, according to the manufacturer's package insert. 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 with TIG (Human) should be given.[1]

Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. is approved for wound management in patients 7 years of age and older.

TABLE 1[1] SUMMARY GUIDE TO TETANUS PROPHYLAXIS IN ROUTINE WOUND MANAGEMENT, FOR PERSONS 7 YEARS OF AGE AND OLDER*

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 **DOSAGE AND ADMINISTRATION** section.

** 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.)

§ Td is preferred by the ACIP to tetanus toxoid alone to enhance diphtheria protection. Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. is approved for wound management in persons 7 years of age or older.

¶ If only three doses of fluid tetanus toxoid have been received, then a fourth dose of toxoid, preferably an adsorbed toxoid should be given.

CONCOMITANT VACCINE ADMINISTRATION

No safety and immunogenicity data are available on the concomitant administration of Tetanus Toxoid Adsorbed manufactured by Aventis Pasteur Inc. with other US licensed vaccines.

HOW SUPPLIED

Vial (latex-free), 1 Dose (10 per package) – Product No. 49281-820-10

Vial, 5 mL – Product No. 49281-800-83

CPT® Code : 90703

CPT is a registered trademark of the American Medical Association.

STORAGE

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

REFERENCES

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10. Institute of Medicine (US). Stratton KR, et al, eds. *Adverse events associated with childhood vaccines: evidence bearing on causality.* Washington (DC*):* National Academy Press. 1994:67-117.
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Product information

as of July 2005

Manufactured by:

Aventis Pasteur Inc.

Swiftwater PA 18370 USA

Aventis Pasteur Aventis