AHFS Category: 80:08

Tetanus and Diphtheria Toxoids Adsorbed

For Adult Use

DECAVAC™

DESCRIPTION

DECAVAC™, Tetanus and Diphtheria Toxoids Adsorbed, For Adult Use (Td), manufactured by Aventis Pasteur Inc. for intramuscular injection, is a sterile suspension of alum-precipitated (aluminum potassium sulfate) toxoids in an isotonic sodium chloride solution. The vaccine, after shaking, is a turbid liquid, whitish-gray in color.

Corynebacterium diphtheriae cultures are grown in a modified Mueller and Miller medium.[1] *Clostridium tetani* cultures are grown in a peptone-based medium containing a bovine extract. The meat used in this medium is US sourced. Tetanus and diphtheria toxins produced during the growth of the cultures are detoxified with formaldehyde. The detoxified materials are then separately purified by serial ammonium sulfate fractionation and diafiltration. DECAVAC vaccine is supplied in a unit dose 0.5 mL preservative-free prefilled syringe presentation, but contains a trace amount of thimerosal [(mercury derivative), (≤ 0.3 µg mercury/dose)] from the manufacturing process.

Each 0.5 mL dose is formulated to contain 5 Lf of tetanus toxoid, 2 Lf of diphtheria toxoid, and not more than 0.28 mg of aluminum by assay. The tetanus and diphtheria toxoids induce at least 2 units and 0.5 units of antitoxin per mL of serum, respectively, in the guinea pig potency test.

CLINICAL PHARMACOLOGY

In the United States (US), immunization against tetanus and diphtheria became widespread in the late 1940s, and resulted in a striking decrease in the incidence of morbidity and mortality from these diseases.

TETANUS

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. The muscle spasms usually involve the jaw (lockjaw) and neck and then become generalized.

The occurrence of tetanus disease in the US decreased steadily from 560 reported cases in 1947 to an average of 43 cases reported annually during 1998-2000. Among patients with known outcome, the case-fatality ratio during 1998-2000 was 18%, 5 times lower than the case-fatality ratio of 91% reported in 1947. In the mid to late 1990s, the age distribution of reported tetanus cases among adults shifted to a younger age group. Among cases reported during 1998-2000, 9% were <20 years of age, 55% were 20-59 years of age, and 36% were =60 years of age. In previous decades, most cases were among persons =60 years of age. Adults =60 years of age continue to have the

highest rates of tetanus and tetanus-related deaths. The majority of tetanus cases during 1998-2000 occurred among persons who were not appropriately vaccinated against tetanus or who had an unknown vaccination history.[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.[3] From 1998 through 2000, one case of neonatal tetanus was reported in the US.[2]

Spores of *C tetani* are ubiquitous. Serologic tests indicate that naturally acquired immunity to tetanus toxin does not occur in the US. Thus, universal primary vaccination, with subsequent maintenance of adequate antitoxin levels by means of appropriately timed boosters, is necessary to protect all age-groups.[3] 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.[4,5] More recently, a level ≥ 0.1 to 0.2 IU/mL has been considered as protective.[6]

DIPHTHERIA

Corynebacterium diphtheriae may cause both localized and generalized disease. The systemic intoxication is caused by diphtheria exotoxin, an extracellular protein metabolite of toxigenic strains of *C diphtheriae.* Both toxigenic and nontoxigenic strains of *C diphtheriae* can cause

disease, but only strains that produce toxin cause myocarditis and neuritis. Toxigenic strains are more often associated with severe or fatal respiratory infections than with cutaneous infections.[3]

Prior to the widespread use of diphtheria toxoid in the late 1940s, diphtheria disease was common in the US. More than 200,000 cases, primarily among children, were reported in 1921. Approximately 5% - 10% of cases were fatal; the highest case-fatality rates were in the very young and the elderly. More recently, reported cases of diphtheria of all types declined from 306 in 1975 to 59 in 1979; most were cutaneous diphtheria reported from a single state. After 1979, cutaneous diphtheria was no longer reportable.[3] From 1980 through 2000, 51 cases of diphtheria were reported in the US, an average of 2 or 3 cases per year. Only one case was reported each year in 1998, 1999, and 2000. The case-fatality rate for diphtheria has changed very little since the 1950s. Of 49 reported cases with known age during the period 1980-2000, 55% were in persons =20 years of age; 43% were among persons =40 years of age.[7] Most cases have occurred in unimmunized or inadequately immunized persons. Although diphtheria disease is rare in the US, it appears that *C diphtheriae* continues to circulate in areas of the country with previously endemic diphtheria.[7]

Diphtheria continues to occur in other parts of the world. A major epidemic of diphtheria occurred in the newly independent states of the former Soviet Union beginning in 1990. This epidemic resulted in approximately 150,000 cases and 5,000 deaths during the years 1990-1998.[8] This outbreak is believed to be due to several factors, including a lack of routine immunization of adults in these countries.[9]

Complete immunization significantly reduces the risk of developing diphtheria and immunized persons who develop disease have milder illness. Protection against disease is due to the development of neutralizing antibodies to diphtheria toxin. A serum antitoxin level of 0.01 IU/mL is the lowest level giving some degree of protection. Antitoxin levels of at least 0.1 IU/mL are generally regarded as protective.[5] Following adequate immunization with diphtheria toxoid, it is thought that protection persists for ≥10 years.[10] Immunization with diphtheria toxoid does not, however, eliminate carriage of *C diphtheriae* in the pharynx, nose, or on the skin.

EFFICACY OF DECAVAC VACCINE

The efficacy of tetanus toxoid and diphtheria toxoid used in DECAVAC vaccine was determined on the basis of immunogenicity studies, with a comparison to a serological correlate of protection (0.01 antitoxin units/mL) established by the Panel on Review of Bacterial Vaccines & Toxoids.[5]

A clinical study to evaluate the serological responses and adverse reactions was performed in 58 individuals 6 years of age and older. The results indicated protective levels of antibody were achieved in greater than 90% of the study population after primary immunization with both components. Booster effects were achieved in 100% of the individuals with pre-existing antibody responses.[11]

No immunogenicity data are available on concomitant administration of DECAVAC vaccine with other US licensed vaccines.

INDICATIONS AND USAGE

DECAVAC vaccine is indicated for active immunization of persons 7 years of age or older for prevention of tetanus and diphtheria. 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).

If passive protection against tetanus is required, Tetanus Immune Globulin (Human) (TIG) may be administered at a separate site with a separate needle and syringe. (See **DOSAGE AND ADMINISTRATION** section, and **Tetanus Prophylaxis in Wound Management** subsection.)

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

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

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine is a contraindication to receipt of DECAVAC vaccine. (See **DESCRIPTION** section.)

It is a contraindication to use DECAVAC vaccine after anaphylaxis or other serious allergic reaction following a previous dose of this vaccine, any other tetanus or diphtheria 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 diphtheria or tetanus components should be carried out. Alternatively, such individuals may be referred to an allergist for evaluation if further immunizations are to be considered.

WARNINGS

A booster dose of Td is recommended at 11-12 years of age if at least 5 years have elapsed since the last dose of tetanus and diphtheria-toxoid containing vaccine.[12] Subsequent routine boosters with Td are recommended every 10 years (see **DOSAGE AND ADMINISTRATION**).[12] More frequent administration of Td is not recommended except under circumstances of wound management or diphtheria prophylaxis (see **DOSAGE AND ADMINISTRATION**) since it may be associated with increased incidence and severity of adverse reactions.[3]

Persons who experienced Arthus-type hypersensitivity reactions or a temperature of >103°F (>39.4°C) following a prior dose of tetanus toxoid usually have high serum tetanus antitoxin levels and should not be given even emergency doses of DECAVAC vaccine more frequently than every 10 years, even if they have a wound that is neither clean nor minor.[3,13]

If Guillain-Barré Syndrome occurred within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the decision to give subsequent doses of DECAVAC vaccine or any vaccine

containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks.[6]

Because of the risk of hemorrhage, DECAVAC vaccine should not be given to persons with any bleeding disorder, such as hemophilia or thrombocytopenia, or to persons on anticoagulant therapy unless the potential benefit clearly outweighs the risk of administration. If the decision is made to administer DECAVAC vaccine in such persons, it should be given with caution, with steps taken to avoid the risk of bleeding and hematoma formation following injection.[3,6]

The Advisory Committee on Immunization Practices (ACIP) has published guidelines for vaccination of persons with recent or acute illness.[6]

PRECAUTIONS

GENERAL

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

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 an injection of any vaccine, all known precautions should be taken to prevent adverse reactions. This includes a review of the patient's previous immunization history, the presence of any contraindications to immunization, the current health status, and history concerning possible sensitivity to the vaccine or similar vaccine. (See **CONTRAINDICATIONS** section.)

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 DECAVAC vaccine.

Administration of Td vaccines is not contraindicated in immunocompromised persons.[6,14]

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 DECAVAC vaccine, health-care providers should inform the patient, parent, or guardian of the benefits and risks of immunization and of the importance of completing the primary immunization series or receiving recommended booster doses, as appropriate.

The health-care provider should inform the patient, parent, or guardian about the potential for adverse reactions that have been temporally associated with the administration of DECAVAC vaccine or other vaccines containing similar components. Parents or guardians, or patients 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).

It is extremely important when the patient returns for a subsequent dose, that the parent, guardian, or patient should be questioned concerning any symptoms and/or signs of an adverse reaction after a previous dose. (See **CONTRAINDICATIONS** and **ADVERSE REACTIONS** Sections).

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

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs and corticosteroids (used in greater than physiologic doses), may reduce the immune response to vaccines (see **PRECAUTIONS** – GENERAL section).

No information is available regarding concomitant administration of DECAVAC vaccine with other US licensed vaccines.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITYNo studies have been performed with DECAVAC vaccine to evaluate carcinogenicity, mutagenic potential, or impact on fertility.

PREGNANCY CATEGORYC

Animal reproduction studies have not been conducted with DECAVAC vaccine. It is also not known whether DECAVAC vaccine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. DECAVAC vaccine should be given to a pregnant woman only if clearly needed.

The ACIP has published recommendations for use of Tetanus and Diphtheria Toxoids Adsorbed For Adult Use in pregnant women.[6]

NURSING MOTHERS

It is not known whether DECAVAC vaccine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when DECAVAC vaccine is administered to a nursing woman.

PEDIATRIC USE

DECAVAC vaccine 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 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).

GERIATRIC USE

Clinical studies of DECAVAC vaccine did not include subjects aged 59 years and over to determine whether they respond differently than younger subjects.

ADVERSE 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 the 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.

In a clinical study involving 58 individuals 6 years of age and older, 19% of the individuals noted local reactions consisting of erythema, tenderness and induration at the injection site and 2% systemic reactions consisting of headache, malaise and temperature elevations.[11]

ADDITIONAL ADVERSE REACTIONS

Additional adverse reactions, included in this section, have been reported in conjunction with receipt of vaccines containing tetanus toxoid and/or diphtheria toxoid.

Arthus-type hypersensitivity reactions, characterized by severe local reactions (generally starting 2-8 hours after an injection), may follow receipt of tetanus toxoid. Such reactions may be associated with high levels of circulating antitoxin in persons who have had overly frequent injections of tetanus toxoid. (See **WARNINGS**.)[15]

Persistent nodules at the site of injection have been reported following the use of adsorbed products.[3]

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 diphtheria and/or tetanus toxoid.[2] Death following vaccine-caused anaphylaxis has been reported.[15]

Certain neurological conditions have been reported in temporal association with some tetanus toxoid-containing vaccines or tetanus and diphtheria 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 Guillain-Barré syndrome.[15] 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 vaccines containing tetanus and/or diphtheria toxoids.[15] In the

differential diagnosis of polyradiculoneuropathies following administration of a vaccine containing tetanus toxoid, tetanus toxoid should be considered as a possible etiology.[15]

POSTMARKETING REPORTS

Additional adverse events reported between 1998-2003 during post-approval use of Tetanus and Diphtheria Toxoids Adsorbed, For Adult Use, manufactured by Aventis Pasteur Inc. include local reactions at injection site (ie, swelling, redness, warmth, cellulitis), myalgia, arthralgia, muscle stiffness, nausea, vomiting, paraesthesia, dizziness, convulsions and rash. Events were included in this list because of the seriousness or frequency of reporting. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequencies or to establish a causal relationship to components of Tetanus and Diphtheria Toxoids Adsorbed, For Adult Use, manufactured by Aventis Pasteur Inc.[16]

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 the occurrence following immunization of any event set forth in the Vaccine Injury Table. For Td vaccines, 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 DECAVAC vaccine package insert.[17,18,19]

Reporting by parents, guardians or patients of all adverse events occurring after vaccine administration should be encouraged. Adverse events following immunization 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. [17,18,19]

Health-care providers should also report these events to the 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 SYRINGE WELL *before administering the vaccine.* The vaccine, after shaking, is a turbid liquid, whitish-gray in color. Discard syringe containing vaccine if the vaccine cannot be resuspended.

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

Inject 0.5 mL 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.

Do not administer this product intravenously or subcutaneously.

The needle length should be sufficient to deliver the vaccine intramuscularly, but not so long as to involve underlying nerves and blood vessels or bone. The health-care professional should determine the appropriate size and length of the needle for individual patients.

PRIMARY IMMUNIZATION

DECAVAC vaccine is approved for administration in persons 7 years of age and older who have not been immunized previously against tetanus and diphtheria, as a primary immunization series of three 0.5 mL doses. For primary immunization with Td vaccines, the intervals between doses recommended by the Advisory Committee on Immunization Practices (ACIP) are 4 to 8 weeks between the first and second dose, and 6 to 12 months between the second and third dose.[3]

DECAVAC vaccine may be used to complete the primary immunization series for tetanus and diphtheria 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 DECAVAC vaccine 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 DECAVAC vaccine. There is no need to start the series over again, regardless of the time elapsed between doses.[3]

Routine Booster Immunization

DECAVAC vaccine is approved for booster immunization in persons 7 years of age and older who have completed primary immunization against tetanus and diphtheria.

A booster dose of Td is recommended by the ACIP in persons 11-12 years of age if at least 5 years have elapsed since the last dose of tetanus and diphtheria toxoid-containing vaccine.[12] Subsequent routine boosters with Td are recommended every 10 years.[12,19] If a dose 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.[3] MORE FREQUENT BOOSTER DOSES ARE NOT RECOMMENDED AND MAY BE ASSOCIATED WITH INCREASED INCIDENCE AND SEVERITY OF ADVERSE REACTIONS.[3,6] (See **WARNINGS** section.)

DIPHTHERIA PROPHYLAXIS FOR CASE CONTACTS

The ACIP has published recommendations on vaccination for diphtheria prophylaxis in individuals who have had contact with a person with confirmed or suspected diphtheria.[3]

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. Individuals 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.[3]

Individuals 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 individuals 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.[3]

Td is the recommended preparation for active tetanus immunization in wound management of patients =7 years of age.[3] In such persons, a preparation containing tetanus and diphtheria toxoids is preferred instead of single-antigen tetanus toxoid to enhance diphtheria protection. DECAVAC vaccine is approved for wound management in patients 7 years of age and older.

TABLE 1[3] 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.

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

† 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.)

§ DECAVAC vaccine is approved for wound management in persons 7 years of age or older.

CONCOMITANT VACCINE ADMINISTRATION

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

HOW SUPPLIED

Luer-Lok® latex-free syringe, 0.5 mL (10 x 0.5 mL syringes per package) – Product No. 49281-291-10

Luer-Lok® is a trademark of Becton Dickinson and Company.

CPT® Code: 90718

CPT is a registered trademark of the American Medical Association.

STORAGE

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

Do not use vaccine after expiration date.

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Product information

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