AHFS Category: 80:08 Rx only

Tetanus and Diphtheria Toxoids Adsorbed

DECAVAC®

DESCRIPTION

DECAVAC®, Tetanus and Diphtheria Toxoids Adsorbed (Td), manufactured by Sanofi Pasteur Inc. for intramuscular injection, is a sterile suspension of alum (aluminum potassium sulfate)-precipitated 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 an extract of bovine muscle tissue. The bovine muscle tissue 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, and adsorbed onto alum.

Each 0.5 mL dose of DECAVAC vaccine is formulated to contain the following active ingredients: 5 Lf of tetanus toxoid and 2 Lf of diphtheria toxoid. 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. Each 0.5 mL dose also contains a trace amount of thimerosal [mercury derivative, (≤0.3 μg mercury/dose) not as a preservative] from the manufacturing process, aluminum adjuvant (not more than 0.28 mg aluminum by assay), and not more than 100 μg (0.02%) of residual formaldehyde.

CLINICAL PHARMACOLOGY

Tetanus

Tetanus is an acute and often fatal disease caused by an extremely potent neurotoxin produced by *C tetani*.

Protection against disease is due to the development of neutralizing antibodies to tetanus toxin. A serum tetanus antitoxin level of 0.01 IU/mL, measured by neutralization assays, is considered the minimum protective level. (2) (3)

Diphtheria

Diphtheria is an acute toxin-mediated disease caused by toxigenic strains of *C diphtheriae.*

Protection against disease is due to the development of neutralizing antibodies to diphtheria toxin. A serum diphtheria antitoxin level of 0.01 IU/mL is the lowest level giving some degree of protection. (3) (4)

Efficacy of DECAVAC vaccine

The efficacy of tetanus toxoid and diphtheria toxoid used in DECAVAC vaccine 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. (3)

A clinical study to evaluate the serological responses and adverse reactions was performed in 58 individuals 6-58 years of age. 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. (5)

INDICATIONS AND USAGE

DECAVAC vaccine is indicated for active immunization for the prevention of tetanus and diphtheria. DECAVAC vaccine is approved for use in persons 7 years of age and older.

CONTRAINDICATIONS

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 (see DESCRIPTION). 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

More frequent administration of DECAVAC vaccine than described in DOSAGE AND ADMINISTRATION may be associated with increased incidence and severity of adverse reactions.

Persons who experienced an Arthus-type hypersensitivity reaction following a prior dose of a tetanus-toxoid containing vaccine usually have high serum tetanus antitoxin levels and should not receive DECAVAC vaccine more frequently than every 10 years, even for tetanus prophylaxis as part of wound management (see DOSAGE AND ADMINISTRATION).

A review by the Institute of Medicine found evidence for a causal relation between tetanus toxoid and both brachial neuritis and Guillain-Barré syndrome. (6) If Guillain-Barré syndrome occurred within 6 weeks after receipt of a prior vaccine containing tetanus toxoid, the decision to give DECAVAC vaccine or any vaccine containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks. (7)

Vaccination with DECAVAC vaccine may not protect all individuals.

PRECAUTIONS

General

Prior to administration of any dose of DECAVAC vaccine, 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, in order to determine the existence of any contraindications to administration of DECAVAC vaccine, and to allow an assessment of the benefits and risks of vaccination.

Epinephrine injection (1:1000) and other appropriate agents and equipment must be immediately available should an acute anaphylactic reaction occur.

Immune responses to inactivated vaccines and toxoids when given to immunocompromised persons may be suboptimal. (7) The immune response to DECAVAC vaccine administered to immunocompromised individuals (whether from disease or treatment) has not been studied.

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 ingredients. Patients, parents or guardians should be

instructed to report any suspected adverse reactions to their health-care professional.

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 DECAVAC vaccine.

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

Carcinogenesis, Mutagenesis, Impairment of Fertility

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

Pregnancy Category C

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.

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 approved for use in infants and children younger than 7 years of age. Safety and effectiveness of DECAVAC vaccine in this age group have not been established.

Geriatric Use

The clinical study that evaluated the immunogenicity and safety of the tetanus and diphtheria toxoids contained in DECAVAC vaccine did not include sufficient numbers of subjects aged 65 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 6-58 years of age, 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. (5)

Data from Post-Marketing Experience

The following adverse events have been spontaneously reported during the post-marketing use of Td manufactured by Sanofi Pasteur Inc. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccination. The following adverse events were included based on severity, frequency of reporting or the strength of causal association to DECAVAC vaccine.

Blood and lymphatic system disorders

Lymphadenopathy.

Immune system disorders

Allergic reactions (such as rash, urticaria, pruritus, and face edema), including anaphylactoid reactions.

Nervous system disorders

Headache, paresthesia, dizziness, syncope, and convulsions.

Gastrointestinal disorders

Nausea, vomiting.

Musculoskeletal, connective tissue and bone disorders

Myalgia, arthralgia, pain in extremities, musculoskeletal stiffness.

General disorders and administration site conditions

Injection site reactions (including swelling, redness, warmth, induration, cellulitis, and nodules).

Pyrexia, chills, pain, malaise, asthenia, fatigue, edema peripheral.

Reporting of Adverse Events

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. (8) The Act further requires the health-care professional to report to the US Department of Health and Human Services the occurrence of certain adverse events following vaccination. (8) For Td, events required to be reported are anaphylaxis or anaphylactic shock within 7 days; brachial neuritis within 28 days; any acute complication or sequelae (including death) of the above events; or any events that would contraindicate further doses of vaccine according to the manufacturer's package insert. (9) These events and other suspected adverse reactions should be reported to the Vaccine Adverse Event Reporting System (VAERS) at 1-800-822-7967 or http://vaers.hhs.gov. Health-care providers should also report adverse events following DECAVAC vaccine to Sanofi Pasteur Inc. at 1-800-822-2463.

DOSAGE AND ADMINISTRATION

Primary Immunization

DECAVAC vaccine may be used 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. The first two doses are administered 4-8 weeks apart and the third dose is administered 6-12 months after the second dose.

DECAVAC vaccine may be used to complete the primary immunization series for tetanus and diphtheria in persons 7 years of age or older who have received one or two doses of Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (whole-cell DTP), Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP) and/or Diphtheria and Tetanus Toxoids Adsorbed (DT). However, the safety and efficacy of DECAVAC vaccine in such regimens have not been evaluated.

Routine Booster Immunization

DECAVAC vaccine may be used for routine booster immunization against tetanus and diphtheria in persons 7 years of age and older who have completed primary immunization against tetanus and diphtheria. Routine booster immunization against tetanus and diphtheria is recommended in children 11-12 years of age and every 10 years thereafter. (7) The Advisory Committee on Immunization Practices (ACIP) has specific recommendations on booster immunization against tetanus and diphtheria for adolescents and adults. (7) (10) (11)

Tetanus Prophylaxis in Wound Management

For active tetanus immunization in wound management of patients 7 years of age and older, a preparation containing tetanus and diphtheria toxoids is preferred instead of single-antigen tetanus toxoid to enhance diphtheria protection. (12) DECAVAC vaccine is approved for wound management of patients 7 years of age and older.

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

When indicated, TIG (Human) should be administered using a separate needle and syringe at a different anatomic site, according to the manufacturer's package insert. If a contraindication to using a tetanus toxoid-containing vaccine exists in a person who has not completed tetanus primary immunization and other than a clean, minor wound is sustained, only passive immunization with TIG (Human) should be given. (12)

Table 1: Summary Guide to Tetanus Prophylaxis in Routine Wound Management for Persons 7 Years of Age and Older (10) (11) (12)

History of Adsorbed Tetanus Toxoid (doses)	Clean, Minor Wounds		All Other Wounds*	
	Td†	TIG	Td†	TIG
Unknown or <three	Yes	No	Yes	Yes
≥ 3‡	No§	No	No‖	No

* 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.

† The ACIP has specific recommendations on use of Td or Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed (Tdap) in adolescents and adults. (10) (11)

‡ 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 the last tetanus toxoid-containing vaccine dose.

‖ Yes, if ≥5 years since the last tetanus toxoid-containing vaccine dose. (More frequent boosters are not needed and can accentuate side effects.)

Diphtheria Prophylaxis for Case Contacts

DECAVAC vaccine may be used for post-exposure diphtheria prophylaxis in persons 7 years of age and older who have not completed primary vaccination, whose vaccination status is unknown, or who have not been vaccinated with diphtheria toxoid within the previous 5 years. Consult

ACIP recommendations for additional interventions for post-exposure diphtheria prophylaxis. (12)

Administration

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

DECAVAC vaccine, after shaking, is a turbid liquid, whitish-gray in color.

For DECAVAC vaccine supplied in vials, shake the vial well before withdrawing the dose. Discard vial if DECAVAC vaccine cannot be resuspended.

For DECAVAC vaccine supplied in syringes, shake the syringe well before administering the dose. Discard syringe if DECAVAC vaccine cannot be resuspended.

Inject 0.5 mL intramuscularly. The preferred site is the deltoid muscle. DECAVAC vaccine should not be injected into the gluteal area or areas where there may be a major nerve trunk.

Do not administer DECAVAC vaccine intravenously or subcutaneously.

DECAVAC vaccine should not be combined through reconstitution or mixed with any other

vaccine.

HOW SUPPLIED

Vial (latex-free), 1 Dose (10 per package) – NDC 49281-291-83

Syringe (latex-free), 1 Dose (10 per package, without needle) – NDC 49281-291-10

STORAGE

Store at 2° to 8°C (35° to 46°F). Do not freeze.

Do not use vaccine after expiration date.

REFERENCES

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Product Information

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