ADACEL®

Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed
Suspension for injection
(For active immunization against Tetanus, Diphtheria and Pertussis)

Route of Administration Intramuscular injection
Dosage Form / Strength Suspension for injection. Each 0.5 mL is formulated to contain:
Active Ingredients Tetanus toxoid, diphtheria toxoid, acellular pertussis [pertussis toxoid (PT), filamentous haemagglutinin (FHA), pertactin (PRN), fimbriae types 2 and 3 (FIM)]
Clinically Relevant Non-medicinal Ingredients Excipients: Aluminum phosphate (adjuvant), 2-phenoxyethanol
Manufacturing process residuals: Formaldehyde and glutaraldehyde are present in trace amounts.
DESCRIPTION ADACEL [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed] is a sterile, uniform, cloudy, white suspension of tetanus and diphtheria toxoids adsorbed separately on aluminum phosphate, combined with acellular pertussis vaccine and suspended in water for injection. The acellular pertussis vaccine is composed of 5 purified pertussis antigens (PT, FHA, PRN and FIM).
INDICATIONS AND CLINICAL USE ADACEL is indicated for: Active booster immunization for the prevention of tetanus, diphtheria and pertussis (whooping cough) in persons 4 years of age and older. Vaccination during pregnancy for passive immunization against pertussis disease in young infants. (See DOSAGE AND ADMINISTRATION, Pregnant Women, and Immunogenicity in Pregnancy.) In children 4 through 6 years of age, ADACEL may be considered as an alternative for the fifth dose of tetanus, diphtheria and acellular pertussis vaccine (DTaP). These children should also receive a separate booster with Inactivated Poliomyelitis Vaccine (IPV) to complete the vaccination series for this age, when indicated.
Persons who have had tetanus, diphtheria or pertussis should still be immunized since these clinical infections do not always confer immunity. (4) Human Immunodeficiency Virus (HIV)-infected persons, both asymptomatic and symptomatic, should be immunized against tetanus, diphtheria and pertussis according to standard schedules. (4) ADACEL is not to be used for the treatment of disease caused by *Bordetella pertussis*, *Corynebacterium diphtheriae* or *Clostridium tetani* infections.
Pediatrics ADACEL is not indicated for immunization of children below the age of 4 years.
Tetanus Prophylaxis in Wound Management The need for active immunization with a tetanus toxoid-containing preparation such as Td Adsorbed vaccine or ADACEL, with or without passive immunization with Tetanus Immune Globulin, depends on both the condition of the wound and the patient's vaccination history. (4) (See DOSAGE AND ADMINISTRATION.)
CONTRAINDICATIONS
Hypersensitivity Known systemic hypersensitivity reaction to any component of ADACEL or a life-threatening reaction after previous administration of the vaccine or a vaccine containing one or more of the same components are contraindications to vaccination. (4) (5) (6) (See SUMMARY PRODUCT INFORMATION.) Because of uncertainty as to which component of the vaccine may be responsible, none of the components should be administered. Alternatively, such persons may be referred to an allergist for evaluation if further immunizations are considered.
Acute Neurological Disorders Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures) within 7 days of a previous dose of a pertussis-containing vaccine not attributable to another identifiable cause is a contraindication to vaccination with any pertussis-containing vaccine (5), including ADACEL.
WARNINGS AND PRECAUTIONS
General Before administration of ADACEL, health-care providers should inform the recipient or the parent or guardian of the recipient of the benefits and risks of immunization, inquire about the recent health status of the recipient, review the recipient's history concerning possible hypersensitivity to the vaccine or similar vaccine, previous immunization history, the presence of any contraindications to immunization and comply with any local requirements regarding information to be provided to the recipient/guardian before immunization. It is extremely important that the recipient, parent or guardian be questioned concerning any signs or symptoms of an adverse reaction after a previous dose of vaccine. (See CONTRAINDICATIONS and ADVERSE REACTIONS.) The rates and severity of adverse events in recipients of tetanus toxoid are influenced by the number of prior doses and level of pre-existing antitoxins. (4) Syncope (fainting) can occur following, or even before, administration of injectable vaccines, including ADACEL. Procedures should be in place to prevent falling injury and manage syncopal reactions. As with any vaccine, ADACEL may not protect 100% of vaccinated persons.
Administration Route Related Precautions: Do not administer ADACEL by intravascular injection: ensure that the needle does not penetrate a blood vessel. Intradermal or subcutaneous routes of administration are not to be utilized. ADACEL should not be administered into the buttocks.
Febrile and Acute Disease: Vaccination should be postponed in cases of an acute or febrile disease. (5) (6) However, a disease with low-grade fever should not usually be a reason to postpone vaccination.
Hematologic Because any intramuscular injection can cause an injection site hematoma in persons with any bleeding disorders, such as hemophilia or thrombocytopenia, or in persons on anticoagulant therapy, intramuscular injections with ADACEL should not be administered to such persons unless the potential benefits outweigh the risk of administration. If the decision is made to administer any product by intramuscular injection to such persons, it should be given with caution, with steps taken to avoid the risk of hematoma formation following injection.
Immune The possibility of allergic reactions in persons sensitive to components of the vaccine should be evaluated. Hypersensitivity reactions may occur following the use of ADACEL even in persons with no prior history of hypersensitivity to the product components. As with all other products, epinephrine hydrochloride solution (1:1,000) and other appropriate agents should be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs. (4) Health-care providers should be familiar with current recommendations for the initial management of anaphylaxis in non-hospital settings, including proper airway management. (4) For instructions on recognition and treatment of anaphylactic reactions, see the current edition of the Canadian Immunization Guide or visit the Health Canada website. Immunocompromised persons (whether from disease or treatment) may not achieve the expected immune response. If possible, consideration should be given to delaying vaccination until after the completion of any immunosuppressive treatment. (4) Nevertheless, vaccination of persons with chronic immunodeficiency such as HIV infection is recommended even if the immune response might be limited. (4) (5)
Neurologic ADACEL should not be administered to individuals with progressive or unstable neurological disorders, uncontrolled epilepsy or progressive encephalopathy until a treatment regimen has been established, the condition has stabilized and the benefit clearly outweighs the risk. (5) (7) (8) If Guillain-Barré syndrome (GBS) occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give ADACEL or any vaccine containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks. (5) (9)
Special Populations
Pregnant Women ADACEL vaccination during pregnancy for passive immunization against pertussis in early infancy has been evaluated in published studies. Safety data from 4 randomized controlled trials (outcomes for 310 pregnancies) (10) (11) (12) (13) and 6 observational studies (outcomes for 125,356 pregnancies) (14) (15) (16) (17) (18) (19) of women who received ADACEL or ADACEL-POLIO during pregnancy (the majority in the 3rd trimester) have shown no vaccine-related adverse effect on pregnancy or on the health of the fetus/newborn child. These studies support the administration of ADACEL during pregnancy (See CLINICAL TRIALS: Immunogenicity in Pregnancy)
Nursing Women The effect of administration of ADACEL during lactation has not been assessed. As ADACEL is inactivated, any risk to the mother or the infant is improbable. However, the effect on breast-fed infants of the administration of ADACEL to their mothers has not been studied. The risks and benefits of vaccination should be assessed before making the decision to immunize a nursing woman.
ADVERSE REACTIONS
Clinical Trial 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 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 of those events. The safety of ADACEL was evaluated in a total of 5,818 participants who received a single dose of ADACEL in 6 clinical trials (298 children ≥4 years of age, 1,508 adolescents, 2,842 adults <65 years of age and 1,170 adults ≥65 years of age). Pain at the injection site was the most common solicited injection site reaction. Most injection site reactions occurred within 3 days following vaccination and their mean duration was less than 3 days. The most frequent systemic reaction was tiredness in children and headache in adolescents and adults (18 - 64 years). Myalgia was the most frequently reported systemic reaction among older adults ≥65 years of age. Fever was reported in less than 10% of vaccinees. These reactions were usually transient and of mild to moderate intensity. In addition, in adolescents and all adults the incidence of injection site and systemic reactions following ADACEL was comparable to those observed with a Td vaccine booster. In children the observed frequencies of injection site reactions and fever following ADACEL were significantly lower than those observed with QUADRACEL (DTaP-IPV) when administered as a booster at 4 to 6 years of age. Except for fever, the observed rates for the systemic reactions were comparable between the two vaccines. Two serious adverse events were reported during Study Td506 which were considered related to the vaccination: a case of severe migraine with unilateral facial paralysis, and a diagnosis of nerve compression in the neck and left arm. Both of these conditions resolved spontaneously or with treatment.
Data from Post-marketing Experience The following additional adverse events have been spontaneously reported during the post-marketing use of ADACEL. 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 vaccine exposure. Decisions to include these events in labelling were based on one or more of the following factors: 1) severity of the event, 2) frequency of reporting, or 3) strength of causal connection to ADACEL.
Immune System Disorders Hypersensitivity (anaphylactic) reaction (angioedema, edema, rash, hypotension)
Nervous System Disorders Paraesthesia, hypoesthesia, Guillain-Barré syndrome, brachial neuritis, facial palsy, convulsion, syncope, myelitis
Cardiac Disorders Myocarditis
Skin and Subcutaneous Tissue Disorders Pruritus, urticaria
Musculoskeletal and Connective Tissue Disorders Myositis, muscle spasm
General Disorders and Administration Site Conditions Large injection site reactions (>50 mm) and extensive limb swelling from the injection site beyond one or both joints have been reported after administration of ADACEL in adolescents and adults. These reactions usually start within 24 - 72 hours after vaccination, may be associated with erythema, warmth, tenderness or pain at the injection site and resolve spontaneously within 3 - 5 days. The risk appears to be dependent on the number of prior doses of acellular pertussis containing vaccine. Injection site bruising, sterile abscess
DRUG INTERACTIONS
Vaccine-Drug Interactions Immunosuppressive treatments may interfere with the development of the expected immune response. (See WARNINGS AND PRECAUTIONS.)
Concomitant Vaccine Administration ADACEL may be administered concurrently with a dose of trivalent inactivated influenza vaccine and with a dose of hepatitis B vaccine in 11 to 12 year-olds. The concomitant use of ADACEL and trivalent inactivated influenza vaccine was evaluated in a clinical trial involving 696 adults 19 to 64 years of age. The safety and immunogenicity profiles in adults that received the vaccines concomitantly were comparable to those observed when the vaccines were given on separate occasions one month apart. (24) The concomitant use of ADACEL and hepatitis B vaccine was evaluated in a clinical trial involving 269 adolescents 11 to 12 years of age. The safety and immunogenicity profiles in adolescents that received the vaccines concomitantly were comparable to those observed when the vaccines were given on separate occasions one month apart. No interference was observed in the immune responses to any of the vaccine antigens when ADACEL and hepatitis B vaccines were given concurrently or separately. (25) Vaccines administered simultaneously should be given using separate syringes at separate injection sites and preferably in separate limbs. ADACEL should not be mixed in the same syringe with other parenterals.
DOSAGE AND ADMINISTRATION
Recommended Dose ADACEL (0.5 mL) should be administered as a booster injection by the intramuscular route. Re-dosing with ADACEL can be used to boost immunity to diphtheria, tetanus and pertussis at 5- to10-year intervals. For re-dosing see Part I Adverse Events for safety at 5 and 10 years and Part II Clinical Trials – Study Td526 – for immunogenicity at 10 years. (26) (27) The preferred site is into the deltoid muscle. Fractional doses (doses <0.5 mL) should not be given. The effect of fractional doses on the safety and efficacy has not been determined. If ADACEL is administered to a pregnant woman, it should ideally be done during the third trimester of pregnancy or according to recommendations from the National Advisory Committee on Immunization (NACI) (3). Health-care professionals should also refer to the NACI recommendations for tetanus prophylaxis in routine wound management. 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 that are minor and uncontaminated, should receive a booster dose of a tetanus toxoid-containing preparation if they have not received tetanus toxoid within the preceding 10 years. For tetanus-prone wounds (e.g., wounds contaminated with dirt, feces, soil and saliva, puncture wounds, avulsions and wounds resulting from missiles, crushing, burns or frostbite), a booster is appropriate if the patient has not received a tetanus toxoid-containing preparation within the preceding 5 years. (4)
Administration Inspect for extraneous particulate matter and/or discolouration before use. (See DESCRIPTION.) If these conditions exist, the product should not be administered.
Shake the vial well until a uniform, cloudy, suspension results. Cleanse the vial stopper with a suitable germicide prior to withdrawing the dose. Do not remove either the stopper or the metal seal holding it in place. Aseptic technique must be used. Use a separate sterile needle and syringe, or a sterile disposable unit for each individual recipient, to prevent disease transmission. Needles should not be recapped but should be disposed of according to biohazard waste guidelines. (See WARNINGS AND PRECAUTIONS.) Before injection, the skin over the site to be injected should be cleansed with a suitable germicide. Administer the total volume of 0.5 mL **intramuscularly** (I.M.). The preferred site of injection is the deltoid muscle. Give the patient a permanent personal immunization record. In addition, it is essential that the physician or nurse record the immunization history in the permanent medical record of each patient. This permanent office record should contain the name of the vaccine, date given, dose, manufacturer and lot number.
OVERDOSAGE For management of a suspected drug overdose, contact your regional Poison Control Centre.
ACTION AND CLINICAL PHARMACOLOGY
Tetanus and Diphtheria: 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. Protection against disease attributable to *C. tetani* 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 assay, is considered the minimum protective level. (5) (6) A tetanus antitoxin level of at least 0.1 IU/mL as measured by the ELISA used in clinical studies of ADACEL is considered as protective for tetanus. Levels of 1.0 IU/mL have been associated with long-term protection. Strains of *C. diphtheriae* that produce diphtheria toxin can cause severe or fatal illness characterized by membranous inflammation of the upper respiratory tract and toxin-induced damage to the myocardium and nervous system. Protection against disease attributable to *C. diphtheriae* 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. (5) (6) Antitoxin levels of at least 0.1 IU/mL are generally regarded as protective. (5) Levels of 1.0 IU/mL have been associated with long-term protection.(6)
Pertussis: Pertussis (whooping cough) is a respiratory disease caused by *B. pertussis*. This Gram-negative coccobacillus produces a variety of biologically active components, though their role in either the pathogenesis of, or immunity to, pertussis has not been clearly defined. The mechanism of protection from *B. pertussis* disease is not well understood. However, in a clinical trial in Sweden (Sweden I Efficacy Trial), the same pertussis components as in ADACEL (i.e., PT, FHA, PRN and FIM) have been shown to prevent pertussis in infants with a protective efficacy of 85.2% using the World Health Organization (WHO) case definition (≥21 consecutive days of paroxysmal cough with culture or serologic confirmation or epidemiological link to a confirmed case). In the same study, the protective efficacy against mild disease was 77.9%. A household contact study that was nested in this efficacy trial demonstrated that there were statistically significant correlations between clinical protection and the presence of antibodies against PT, PRN and FIM in pre-exposure sera. (28) Minimum serum antibody levels to specific pertussis vaccine components that confer protection against the development of clinical pertussis have not been identified. Nevertheless, a number of studies have demonstrated a correlation between the presence of serum antibody responses to pertussis vaccine components and protection against clinical disease. In ADACEL clinical trials, in children, adolescents and adults <65 years of age, post-vaccination Geometric Mean Concentrations (GMCs) for all pertussis antibodies were consistently above those of TRIPACEL in the Sweden I Efficacy Trial. (20) (21) (24) (25) (29) Older adults (≥65 years of age) vaccinated with a single dose of ADACEL achieved lower GMCs for some of the pertussis antibodies than did infants who had received 3 or 4 doses of TRIPACEL. Nevertheless, their post-immunization anti-pertussis antibody levels were 4.4- to 15.1-fold higher than pre-immunization levels, suggested an improved degree of protection against pertussis. (23)
STORAGE AND STABILITY Store at 2° to 8°C (35° to 46°F). **Do not freeze**. Discard product if exposed to freezing (≤ 0°C). ADACEL has been shown to remain stable at temperature above 8°C and up to 25°C, for a maximum of 3 days (72 hours). These data are not recommendations for shipping or storage, but may guide decision for use in case of temporary temperature excursions. Do not use after expiration date.
DOSAGE FORMS, COMPOSITION AND PACKAGING
Dosage Forms ADACEL is supplied as a sterile uniform, cloudy, white suspension in a vial.
Composition Each single dose (0.5 mL) contains:
Active Ingredients Tetanus Toxoid 5 Lf Diphtheria Toxoid 2 Lf Acellular Pertussis Pertussis Toxoid (PT) 2.5 µg Filamentous Haemagglutinin (FHA) 5 µg Pertactin (PRN) 3 µg Fimbriae Types 2 and 3 (FIM) 5 µg
Other Ingredients *Excipients* Aluminum Phosphate (adjuvant) 1.5 mg 2-phenoxyethanol 0.6% v/v *Manufacturing Process Residuals* Formaldehyde and glutaraldehyde are present in trace amounts.
Packaging ADACEL is supplied in 0.5 mL single dose glass vials. The vials are made of Type 1 glass. The container closure system of ADACEL is free of latex (natural rubber).
ADACEL is available in a package of: 1 single dose vial
Product information as of March 2021.
Manufactured by: **Sanofi Pasteur Limited** Toronto, Ontario, Canada

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