Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed

ADACEL®

Intramuscular injection

Suspension for injection

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) as a single dose in persons aged 11 to 54 years.

Persons who have had tetanus, diphtheria or pertussis should still be immunized since these clinical infections do not always confer immunity. Human Immunodeficiency Virus (HIV)-infected persons, both asymptomatic and symptomatic, should be immunized against tetanus, diphtheria and pertussis according to standard schedules.

ADACEL® is not to be used for the treatment of disease caused by *B. pertussis, C. diphtheriae* or *C. tetani* infections.

Other Populations:

ADACEL® is not indicated for immunization of children below the age of 11 years and in persons above the age of 54 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. (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. (See DOSAGE FORMS, COMPOSITION AND PACKAGING.) 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, 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.

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. 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. Health-care providers should be familiar with current recommendations for the initial management of anaphylaxis in non-hospital settings, including proper airway management.

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. Nevertheless, vaccination of persons with chronic immunodeficiency such as HIV infection is recommended even if the immune response might be limited.

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.

A review by the US Institute of Medicine (IOM) found evidence for a causal relation between tetanus toxoid and both brachial neuritis and Guillain-Barré syndrome (GBS). If 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.

A few cases of demyelinating diseases of the central nervous system, peripheral mononeuropathies and cranial mononeuropathies have been reported following vaccines containing tetanus and/or diphtheria toxoids, although the IOM concluded that the evidence is inadequate to accept or reject a causal relation between these conditions and vaccination.

Pregnant Women

The effect of ADACEL® on the development of the embryo and fetus has not been assessed. Vaccination in pregnancy is not recommended unless there is a definite risk of acquiring pertussis. As the vaccine is inactivated, risk to the embryo or the fetus is improbable. The benefits versus the risks of administering ADACEL® during pregnancy should be carefully evaluated when there is a high probable risk of exposure to a household contact or during an outbreak in the community.

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 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 of those events.

The safety of ADACEL® was evaluated in a total of 4,648 participants who received a single dose of ADACEL® in 5 clinical trials (including 1,508 adolescents and 2,842 adults).

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 and headache in adolescents and adults. 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 adults the incidence of injection site and systemic reactions following ADACEL® was comparable to those observed with a Td vaccine booster.

Table 1: Frequency (%) of Solicited Adverse Events Observed Within 0 to 14 Days in Clinical Trials in Adolescents and Adults, Following a Single Dose with ADACEL®

Solicited Reactions	Adolescents (N = 1,184)	Adults (N = 1,752)
Injection Site Reactions		
Pain	77.8	65.7
Swelling	20.9	21.0
Erythema	20.8	24.7
Systemic Reactions		
Fever (≥38.0°C)	5.0	1.4
Headache	43.7	33.9
Nausea	13.3	9.2
Diarrhea	10.3	10.3
Vomiting	4.6	3.0
Anorexia	N.S*	N.S*
Rash	2.7	2.0
Body Ache or Muscle Weakness	30.4	21.9
Sore or Swollen Joints	11.3	9.1
Tiredness	30.2	24.3
Chills	15.1	8.1
Axillary Lymph Node Swelling	6.6	6.5

* Not solicited

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.

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.

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

The immunization schedule with ADACEL® should follow local recommendations. ADACEL® should be administered as a single injection of 1 dose (0.5 mL) by the intramuscular route. 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.

The use of ADACEL® in management of tetanus-prone wounds should follow local recommendations. Canada's NACI and US ACIP have issued guidelines for tetanus prophylaxis in routine wound management as shown in Table 2.

Table 2: NACI Recommended Use of Immunizing Agents in Wound Management

History of Tetanus Immunization	Clean, Minor Wounds		All Other Wounds	
	Td*	TIG† (Human)	Td*	TIG† (Human)
Uncertain or <3 doses of an immunization series‡	Yes	No	Yes	Yes
≥3 doses received in an immunization series‡	No§	No	No**	No††

* Adult-type tetanus and diphtheria toxoid.

† Tetanus immune globulin, given at a separate site from the Td.

‡ Primary immunization is at least 3 doses at age appropriate intervals.

§ Yes, if >10 years since last booster.

** Yes, if >5 years since last booster.

†† Yes, if persons are known to have a significant humoral immune deficiency state (e.g., HIV, agammaglobulinemia) since immune response to tetanus toxoid may be suboptimal.

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.

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** (IM). The preferred site of injection is the deltoid muscle.

STORAGE AND STABILITY

Store at 2° to 8°C. **Do not freeze**. Discard product if exposed to freezing. 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
5 single dose vials

Shelf life of the vaccine: 36 months

Product information as of September 2014.

Manufactured by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

Imported and Marketed in India by:
Sanofi Pasteur India Private Limited
EI-223, T.T.C. Industrial Area
Mahape, Navi Mumbai, Dist. Thane 400710

Registered Office:
Sanofi Pasteur India Private Limited
Sanofi House, CTS No. 117-B
L&T Business Park
Saki Vihar Road, Powai
Mumbai 400072

Warning: To be sold by retail on the prescription of the Registered Medical Practitioner.

Version 2 updated in Oct 2019

R1-1019 India
D54-190CF
769292-306