For the use of a Registered Medical Practitioner Only

Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed

ADACEL®
Intramuscular injection
Suspension for injection

DESCRIPTION:

ADACEL® is supplied as a sterile uniform, cloudy, white suspension in a vial.

Each dose (0.5 mL) is formulated to contain: Tetanus Toxoid (5 Lf); Diphtheria Toxoid (2 Lf); Acellular Pertussis [Pertussis Toxoid (PT), 2.5 mcg; Filamentous Haemagglutinin (FHA), 5 mcg; Pertactin (PRN), 3 mcg and Fimbriae Types 2 and 3 (FIM), 5 mcg].

The non-medicinal ingredients are as follows: Aluminum Phosphate (1.5 mg) and 2-phenoxyethanol (0.6% v/v). 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

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

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.

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 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.
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

Adverse Reaction Overview

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.

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.

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Table 2: Frequency (%) of Solicited Reactions Observed Within 0 to 14 Days in Clinical Trials in Children, Adolescents and Adults, Following a Single Dose With ADACEL®

Solicited Reactions	**Children 4 - 6 years (N = 298)**	**Adolescents 11 - 17 years (N = 1,184)**	**Adults 18 - 64 years (N = 1,752)**	**Adults ≥65 years (N = 1,153)**
Injection Site Reactions				
Pain	39.6	77.8	65.7	43.0

Swelling	24.2	20.9	21.0	18.1
Erythema	34.6	20.8	24.7	24.3
Systemic Reactions				
Fever (≥38.0°C)	8.7	5.0	1.4	0.5
Headache	16.4	43.7	33.9	18.2
Nausea	9.4	13.3	9.2	N.S.*
Diarrhea	14.4	10.3	10.3	N.S.*
Vomiting	8.1	4.6	3.0	N.S.*
Anorexia	21.5	N.S.*	N.S.*	N.S.*
Rash	8.4	2.7	2.0	N.S.*
Body Ache or Muscle Weakness † / Myalgia‡	6.4	30.4	21.9	28.4
Sore or Swollen Joints	4.0	11.3	9.1	N.S.*
Tiredness§ / Malaise**	31.5	30.2	24.3	17.2
Chills	7.1	15.1	8.1	N.S.*
Axillary Lymph Node Swelling	5.4	6.6	6.5	N.S.*

* Not Solicited

† Body ache or muscle weakness was the solicited term in the trials in children, adolescents and adults 18 - 64 years of age.

‡ Myalgia was the solicited term in the trial in adults ≥65 years of age.

§ Tiredness was the solicited term in the trials in children, adolescents and adults 18 - 64 years of age.

** Malaise was the solicited term in the trial in adults ≥65 years of age.

Post-Market Adverse Reactions 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

Drug-Drug Interactions

Vaccine-Drugs 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

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.

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 1: 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]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** (I.M.). 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 (≤ 0°C).

DOSAGE FORM, COMPOSITION & PACKAGING

ADACEL® is supplied as a sterile uniform, cloudy, white suspension in a vial.

COMPOSITION

Each 0.5mL contains:
Tetanus Toxoid Adsorbed .....5 Lf
Diphtheria Toxoid Adsorbed .....2 Lf
Pertussis Toxoid Adsorbed (PT) .....2.5 micrograms (µg)
Filamentous Haemagglutinin Adsorbed (FHA) .... 5.0 micrograms (µg)
Pertactin Adsorbed (PRN) ..... 3.0 micrograms (µg)
Fimbriae Types 2 and 3 Adsorbed (FIM) ..... 5.0 micrograms (µg)
Aluminium Phosphate (Adjuvant) .....1.5 milligram (mg)
2-Phenoxyethanol ..... 0.6 %v/v
Formaldehyde ..... 5.0000 micrograms (µg)
Glutaraldehyde-Trace Amounts
Water for Injection .....q.s. 0.5 ml

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
Not all presentations maybe marketed

SHELF LIFE OF THE VACCINE: 48 months

Manufactured by:
Sanofi Pasteur Limited
1755 Steeles Avenue West
Toronto Ontario (Canada)
M2R3T4

Imported & Marketed in India by:
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