ADACEL™

SAMPLE

Tetanus and Diphtheria Toxoids Adsorbed
Combined with Component Pertussis Vaccine

COMPOSITION

Each dose (0.5 mL) contains:

tetanus toxoid	5 Lf
diphtheria toxoid	2 Lf
component pertussis	
pertussis toxoid	2.5 µg
filamentous haemagglutinin	5 µg
fimbrial agglutinogens 2 + 3	5 µg
pertactin	3 µg
aluminium phosphate (aluminum 0.33 mg)	1.5 mg
2-phenoxyethanol	0.6% (v/v)
residual formaldehyde	≤5 µg
residual glutaraldehyde	<50 ng

ADACEL™ appears as a sterile, uniform, cloudy, white suspension.

PHARMACEUTICAL CLASSIFICATION

Combination vaccine (suspension), for administration by the intramuscular route

INDICATIONS

ADACEL™ is indicated for active booster immunization for the prevention of tetanus, diphtheria and pertussis in children, adolescents and adults aged11 to 64 years.

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

CONTRAINDICATIONS

Known systemic hypersensitivity to any component of ADACEL™ after previous administration of the vaccine or a vaccine containing the same substances are contraindications to vaccination.

Encephalopathy not attributable to another identifiable cause within 7 days of administration of a previous dose of any vaccine containing pertussis antigens (whole-cell or acellular pertussis vaccines) is a contraindication to vaccination.

Pertussis vaccine should not be administered to individuals with progressive neurological disorders, uncontrolled epilepsy, or progressive encephalopathy until a treatment regimen has been established, the condition has been stabilized and the benefit clearly outweighs the risk.

Postponement of vaccination should be considered in case of febrile or acute illness. However, a minor febrile or non-febrile illness, such as a mild upper respiratory infection is not usually a reason to postpone immunization.

PREGNANCY AND LACTATION

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 highly improbable. The benefits versus the risks of administering ADACEL™ in pregnancy should carefully be evaluated when there is a high probable risk of exposure to a household contact or during an outbreak in the community.

The effect of administration of ADACEL™ during lactation has not been assessed. As ADACEL™ is inactivated, any risks to the mother or the infant is highly improbable. The benefits versus the risks of administering ADACEL™ during lactation should carefully be evaluated by the health-care provider, particularly when there is a high probable risk of disease transmission through exposure to a household contact, or during an outbreak in the community. The risk of disease transmission from the infected mother to the infant who may not have been fully immunized should also be evaluated.

WARNINGS AND PRECAUTIONS

Intramuscular injections should be given with care in patients suffering from coagulation disorders or on anticoagulant therapy.

ADACEL™ should not be administered into the buttocks, nor by the intradermal route.

Do not administer by intravascular injection, ensure that the needle does not penetrate a blood vessel.

The use of fractional doses in an attempt to reduce the severity of adverse reactions is not recommended because there is insufficient evidence on the safety or efficacy of such smaller doses.

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.

The possibility of allergic reactions in persons sensitive to components of the vaccine should be evaluated. Allergic reactions may occur following the use of ADACEL™ even in persons with no prior history of hypersensitivity to the product components.

Arthus-type hypersensitivity reactions, characterized by severe local reactions (generally starting 2 to 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.

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of prior vaccine containing tetanus toxoid, the decision to give any vaccine containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks.

It is extremely important that the patient, parent or guardian be questioned concerning any symptoms and/or signs of an adverse reaction after a previous dose of vaccine. (See ADVERSE EFFECTS.)

Aseptic technique must be used. Use a separate sterile needle and syringe, or a sterile disposable unit for each individual patient to prevent disease transmission. Needles should not be recapped but should be disposed of according to biohazard waste guidelines.

Immunocompromised persons (whether from disease or treatment) may not obtain the expected immune response. If possible, consideration should be given to delaying vaccination until after the completion of any immunosuppressive treatment. Nevertheless, vaccination of subjects with chronic immunodeficiency such as HIV infection is recommended even if the immune response might be limited.

As with any vaccine, immunization with ADACEL™ may not protect 100% of susceptible persons.

Before administration of any dose of ADACEL™, the parent or guardian of the recipient or the adult recipient must be asked about personal history, family history and recent health status, including immunization history, current health status and any adverse event after previous immunizations. In persons who have a history of serious or severe reaction within 48 hours of a previous injection with a vaccine containing similar components, the course of the vaccination must be carefully considered.

Before the injection of any biological, the person responsible for administration must take all precautions known for the prevention of allergic or any other reactions. As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following administration of the vaccine.

CONCURRENT ADMINISTRATION

ADACEL™ may be administered concurrently with a dose of inactivated influenza vaccine at separate sites with separate syringes.

ADACEL™ may be administered concurrently with a dose of Hepatitis B vaccine in 11 and 12 year-olds at separate sites with separate syringes.

Because simultaneous administration of common vaccines is not known to affect the efficacy or safety of any of the routine recommended vaccines, if return of a patient for further immunization is doubtful, simultaneous administration of all vaccines appropriate for age and previous vaccination status (including IPV, MMR) at separate sites with separate syringes is indicated. Vaccines containing acellular pertussis may be administered simultaneously with other inactivated and live vaccines at different sites.

If any other vaccines are administered during the same visit, they must be given at separate sites with separate syringes.

ADACEL™ should not be mixed in the same syringe with other parenterals.

INSTRUCTIONS FOR USE

The vaccine's normal appearance is a uniform, cloudy, white suspension.

Inspect for extraneous particulate matter and/or discoloration before use. If these conditions exist, the product should not be administered.

Just before use, shake the vial well until a uniform, cloudy suspension results. When withdrawing a dose from a stoppered vial, do not remove either the stopper or the metal seal holding it in place. Aseptic technique must be used for withdrawl of the dose. (See WARNINGS AND PRECAUTIONS.)

Withdraw and inject a 0.5 mL dose. The preferred site is into the deltoid muscle. Do not administer intravenously.

Needles should not be recapped and should be disposed of properly.

POSOLOGY

ADACEL™ should be administered as a single injection of one dose (0.5 mL) by the intramuscular route. The preferred site is into the deltoid muscle.

There are currently no data upon which to base a recommendation for the optimal interval for administering subsequent booster doses with ADACEL™.

For individuals planning to travel to developing countries, it may be prudent to offer an early tetanus booster, before travel, if more than 5 years have elapsed since the last dose.

Tetanus Prophylaxis in Wound Management

The table below summarizes the recommended use of immunizing agents in wound management. It is important to ascertain the number of doses of tetanus toxoid previously given and the interval since the last dose. When a tetanus booster dose is required, a combined preparation of tetanus and diphtheria toxoid formulated for adults (Td) is preferred. Appropriate cleansing and debridement of the wound is imperative and use of antibiotics may be considered.

History of tetanus immunization	Clean, minor wounds Td*	Clean, minor wounds TIG† (Human)	All other wounds Td	All other wounds 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 toxoids.
† 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 individuals are known to have a significant humoral immune deficiency state (e.g., HIV, agammaglobulinemia) since immune response to tetanus toxoid may be suboptimal.

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.

ADVERSE EFFECTS

Safety Data from Clinical Trials

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™ has been evaluated in a total of 3,952 participants who received a single dose of ADACEL™ in 4 clinical trials (298 children ≥4 years of age, 1,508 adolescents and 2,146 adults).

Pain at the injection site was the most common local adverse event. Most injection site reactions occurred within 3 days following vaccination and their mean duration was less than 3 days. The most frequent systemic adverse event was tiredness in children and headache in adolescents and adults. Fever was reported in less than 10%. These adverse events were usually transient and of mild to moderate intensity. In addition, in adolescents and adults the incidence of local and systemic adverse events following ADACEL™ was comparable to those observed with a Td vaccine booster. In children the observed frequencies of local adverse events 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 adverse events were comparable between the two vaccines. The frequency of the solicited local and systemic adverse events reported in two clinical trials are shown in Table 1.

TABLE 1: FREQUENCY (%) OF SOLICITED ADVERSE EVENTS OBSERVED WITHIN 0 TO 14 DAYS IN CLINICAL TRIALS IN CHILDREN, ADOLESCENTS AND ADULTS, FOLLOWING A SINGLE DOSE WITH ADACEL™

Adverse Event	Children (N = 298)	Adolescents (N = 1,184)	Adults (N = 1,752)
General Disorders and Administration Site Conditions			
Injection Site Pain	39.6	77.8	65.7
Tiredness	31.5	30.2	24.3
Injection Site Swelling	24.2	20.9	21.0
Injection Site Erythema	34.6	20.8	24.7
Chills	7.1	15.1	8.1
Axillary Lymph Node Swelling	5.4	6.6	6.5
Fever (≥38.0°C)	8.7	5.0	1.4
Skin and Subcutaneous Disorders			
Rash	8.4	2.7	2.0
Nervous System Disorders			
Headache	16.4	43.7	33.9
Musculo-Skeletal and Connective Tissue Disorders			
Body Ache or Muscle Weakness	6.4	30.4	21.9
Sore or Swollen Joints	4.0	11.3	9.1
Gastrointestinal Disorders			
Nausea	9.4	13.3	9.2
Diarrhea	14.4	10.3	10.3
Vomiting	8.1	4.6	3.0

Data from Post-Marketing Experience

The following 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 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) seriousness of the event, 2) frequency of reporting, or 3) strength of causal connection to ADACEL™.

The following adverse events were included based on severity, frequency of reporting and the strength of causal association to ADACEL™.

General disorders and administration site conditions:
- injection site bruising, sterile abscess

Skin and subcutaneous tissue disorders:
- pruritus, urticaria

There have been serious spontaneous reports of nervous system disorders such as myelitis, syncope vasovagal, paresthesia, hypoesthesia and musculoskeletal and connective tissue disorders such as myositis and muscle spasms temporally associated with ADACEL™.

Additional Adverse Reactions

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

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

Cases of allergic or anaphylactic reaction (i.e., hives, swelling of the mouth, difficulty breathing, hypotension, or shock) have been reported after receiving some preparations containing diphtheria, tetanus toxoids and/or pertussis antigens. Death following vaccine-caused anaphylaxis has been reported.

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 US 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. 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. In the differential diagnosis of polyradiculoneuropathies following administration of a vaccine containing tetanus toxoid, tetanus toxoid should be considered as a possible etiology.

PRECAUTIONS FOR USE

KEEP OUT OF REACH OF CHILDREN.

STORAGE

Store at 2° to 8°C. DO NOT FREEZE. Discard product if exposed to freezing. Do not use after expiration date.

HOW SUPPLIED

Vial 1 x 0.5 mL (Single Dose) Vial 5 x 0.5 mL (Single Dose)

Product Information as of November 2006.

Manufactured by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

On Medical Prescription Only

Imported by
PT Aventis Pharma,
Jakarta, Indonesia
Reg.

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