AUSTRALIAN PRODUCT INFORMATION

NAME OF THE MEDICINE

ADACEL®

Pertussis Vaccine-Acellular Combined with Diphtheria and Tetanus Toxoids (Adsorbed)

DESCRIPTION

ADACEL is a sterile, uniform, cloudy, white suspension for injection.

Each 0.5 mL dose of ADACEL contains:

2.5 µg	pertussis toxoid
5 µg	pertussis filamentous haemagglutinin
5 µg	pertussis fimbriae types 2 and 3
3 µg	pertussis pertactin
≥ 2 IU (2 LfU)	diphtheria toxoid
≥ 20 IU (5 LfU)*	tetanus toxoid
1.5 mg	aluminium phosphate (equivalent to 0.33mg aluminium)
0.6% v/v	phenoxyethanol
≤ 0.005mg	formaldehyde
≤ 0.02mg	glutaraldehyde

water for injections to 0.5mL

*The formulated content of 5LfU per 0.5mL dose of tetanus toxoid is the same as the related product Tripacel®.

The vaccine is prepared from: adsorbed purified and formaldehyde detoxified diphtheria and tetanus toxins; adsorbed purified and glutaraldehyde detoxified pertussis toxin (pertussis toxoid or PT); adsorbed purified and formaldehyde treated filamentous haemagglutinin (FHA); adsorbed purified pertactin (PRN) and fimbriae types 2 and 3 (FIM).

ADACEL is an adult/adolescent formulation diphtheria-tetanus-acellular pertussis (dTpa) combination vaccine with reduced content of pertussis toxoid, filamentous haemagglutinin and diphtheria toxoid compared to paediatric diphtheria-tetanus-acellular pertussis (DTaP) formulations.

The manufacture of this product includes exposure to bovine materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

PHARMACOLOGY

Clinical Trials

A total of 962 individuals (324 adolescents and 638 adults), who had not been immunised against tetanus, diphtheria, or pertussis within the previous five years, received a single 0.5 mL dose of ADACEL in three clinical trials (TC9704, TD9805 and TC9707).

In TC9704, 449 (55 adolescents 12 to 17 years of age and 394 adults 18 to 54 years of age) received three lots of ADACEL (dTpa), while 300 (37 adolescents and 263 adults) were given a single 0.5 mL dose with an adult formulation diphtheria-tetanus vaccine (Td) and a monovalent acellular Pertussis (aP) vaccine, given separately, one month apart. In TD9805, 269 adolescents 11 to 12 years of age were vaccinated: 135 received ADACEL given alone followed by the first dose of a 3-dose primary series with Hepatitis B vaccine (HB), one month later, and 134 were given ADACEL concurrently with the first dose of HB.

In TC9704, the safety and immunogenicity profile of ADACEL was shown to be comparable to that observed with a single booster dose of Td and aP containing the same amount of tetanus and diphtheria toxoids and pertussis antigens, administered separately. In TD9805, the safety and immunogenicity of concomitant administration of Hepatitis B vaccine with ADACEL (dTpa+HB) was comparable to that observed with ADACEL alone. Antibody responses observed in adolescents and adults from TD9805 and TC9704 are presented in the tables below:

	TD9805 11 to 12 years				TC9704 12 to 54 years			
Antitoxin	**Vaccine**	**N**	**GMC**	**% ≥0.10 IU/mL***	**Vaccine**	**N**	**GMC**	**% ≥0.10 IU/mL***
Tetanus	**dTpa**	118	28.6	100.0	**dTpa**	446	15.7	100.0
	dTpa+HB	129	26.1	100.0	**Td**	151	16.0	99.3
Diphtheria	**dTpa**	118	8.4	100.0	**dTpa**	446	0.8	85.0
	dTpa+HB	129	6.8	100.0	**Td**	151	1.2	89.4

* Tetanus and diphtheria antitoxin levels were measured in EU and IU/mL, respectively

	TD9805 11 to 12 years			TC9704 12 to 54 years		
Pertussis Antibody	**Vaccine**	**N**	**GMC****	**Vaccine**	**N**	**GMC**
Anti-PT	**dTpa**	118	169	**dTpa**	445	144
	dTpa+HB	129	144	**aP**	149	191
Anti-FHA	**dTpa**	118	445	**dTpa**	446	328
	dTpa+HB	129	375	**aP**	149	349
Anti-PRN	**dTpa**	118	280	**dTpa**	446	279
	dTpa+HB	129	303	**aP**	149	191
Anti-FIM	**dTpa**	118	1033	**dTpa**	446	995
	dTpa+HB	129	1130	**aP**	149	1825

** All GMCs (Geometric Mean Concentrations) are in EU/mL

In TD9707, 244 adults (19 to 60 years of age) received ADACEL, while 126 received Td and aP, given separately, one month apart. The safety and immunogenicity profile of ADACEL was also shown to be comparable to that observed with a single booster dose of Td and aP in study TD9707.

The mechanism of protection from *B pertussis* disease is not well understood. In a pertussis efficacy trial conducted in Sweden between 1992 and 1995, primary immunisation with Sanofi Pasteur Limited's acellular pertussis infant DTaP formulation conferred a protective efficacy of 85% against typical pertussis disease (WHO definition). Although ADACEL contains only one quarter of the amount of pertussis toxoid present in this acellular pertussis infant DTaP formulation, the antibody responses to ADACEL were superior to those observed in the pertussis efficacy trial.

INDICATIONS

ADACEL is indicated for active immunisation against tetanus, diphtheria and pertussis in persons aged 10 years and over as a booster following primary immunisation.

CONTRAINDICATIONS

ADACEL should not be administered to individuals who have previously had a hypersensitivity reaction to any vaccine containing diphtheria or tetanus toxoids, or pertussis (acellular or whole cell).

ADACEL should not be administered to individuals known to be hypersensitive to any component of the vaccine (see components listed in DESCRIPTION) or residues carried over from manufacture (such as formaldehyde and glutaraldehyde).

ADACEL should not be administered to subjects who experienced an encephalopathy of unknown origin within 7 days of previous immunisation with a pertussis-containing vaccine, or to subjects who have experienced other neurological complications following previous immunisation with any of the antigens in ADACEL.

PRECAUTIONS

The use of ADACEL as a primary series, or to complete the primary series, has not been studied. A booster response will only be elicited in individuals who have been previously primed by vaccination. Individuals with an incomplete, or no, history of a primary series of diphtheria and tetanus toxoids should not be vaccinated with ADACEL.

Diphtheria and tetanus toxoid containing vaccines should be avoided in persons who have received a booster with a vaccine containing these toxoids within the previous five years because of the potential increased frequency of local adverse reactions.

There are currently no data upon which to base a recommendation for the optimal interval for administering subsequent booster doses with ADACEL to maintain antibody levels against pertussis. There are no data on the duration of protection against pertussis following vaccination with ADACEL.

As with all injectable vaccines, appropriate medical treatment and supervision should be readily available for immediate use in case of a rare anaphylactic reaction following the administration of vaccine. As a precautionary measure, adrenaline injection (1:1,000) must be immediately available in case of unexpected anaphylactic or serious allergic reactions.

The vaccine must be given intramuscularly, as subcutaneous administration increases the chances of a local reaction. Do not administer by intravascular injection. A persistent nodule at the site of injection may occur with all adsorbed vaccines particularly if administered into the superficial layers of the subcutaneous tissue.

Intramuscular injections should be given with care in patients suffering from coagulation disorders because of the risk of haemorrhage. In these situations administration of ADACEL by deep subcutaneous injection may be considered, although there is a risk of increased local reactions.

ADACEL should not be administered into the buttocks due to the varying amounts of fatty tissue in this region, nor by the intradermal route, since these methods of administration may induce a weaker immune response.

Formaldehyde and glutaraldehyde have been used in the manufacturing process of this product and trace residual amounts may be present in the final product. Therefore, a hypersensitivity reaction may occur.

If Guillain-Barré syndrome or brachial neuritis has occurred following 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.

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 stabilised and the benefit clearly outweighs the risk.

The immunogenicity of the vaccine could be reduced by immunosuppressive treatment or immunodeficiency. It is recommended to postpone the vaccination until the end of such disease or treatment if practical.

Nevertheless, vaccination of HIV infected subjects or subjects with chronic immunodeficiency, such as AIDS, is recommended even if the antibody response might be limited.

As with any vaccine, immunisation with ADACEL may not protect 100% of susceptible individuals.

Vaccination should be deferred in the presence of any acute illness. A minor illness with a current temperature below 38.5°C, such as mild upper respiratory infection, is not usually a reason to defer immunisation.

Effects on Fertility

ADACEL has not been evaluated for the possible effects on fertility.

Use in pregnancy (Category B2)

The effect of ADACEL on the development of the embryo and foetus has not been assessed. Vaccination in pregnancy is not recommended unless there is a definite risk of acquiring pertussis. As the vaccine is detoxified, risk to the embryo or the foetus 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.

Use in lactation

The effect of administration of ADACEL during lactation has not been assessed. As ADACEL is detoxified, any risk 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 risks of disease transmission from the infected mother to the infant who may not have been fully immunised should also be evaluated.

Genotoxicity

ADACEL has not been tested for genotoxic potential.

Carcinogenicity

ADACEL has not been tested for carcinogenic potential.

Use in children

ADACEL should not be used for primary immunisation.

ADACEL is indicated for use in children aged 10 years and over.

INTERACTIONS WITH OTHER MEDICINES

ADACEL can be administered concomitantly with Hepatitis B vaccine, using a separate limb for the site of injection. Concomitant administration of other vaccines with ADACEL has not been studied.

In the case of immunosuppressive therapy, refer to PRECAUTIONS.

ADVERSE EFFECTS

The reactions are listed within body systems and categorised by frequency according to the following definitions:

Very common	(≥ 1/10)
Common	(< 1/10 and ≥ 1/100)

Uncommon (< 1/100 and ≥ 1/1,000)

Clinical Trial Experience

In clinical studies with 324 adolescents and 638 adults given ADACEL, the most frequently reported adverse reactions occurring during the first 24 hours included the following:

Very common	Pain, swelling, redness at the injection site
	Headache, decreased energy, generalised body-ache
Common	Fever, chills, nausea, diarrhoea, sore or swollen joints
Uncommon	Vomiting

A causal relationship to vaccination was not established in all cases. All adverse reactions were generally mild and transient in duration. Fever was reported in less than 3% of vaccinees. There were no reports of fever over 39.9 °C. This adverse reaction profile was shown to be comparable to that seen in vaccinees who received a booster with Td adsorbed vaccine (tetanus (5 LfU) and diphtheria (2 LfU) toxoids adsorbed). Late-onset local adverse reactions (i.e. a local adverse reaction which had an onset or increase in severity 3 to 8 days post-immunisation) such as redness, swelling and pain, occurred in less than 2%.

The following table summarises Adverse Events (%) in ADACEL (dTpa) recipients 0 - 24 hours post vaccination:

	ADOLESCENTS**			**ADULTS**	
Event	**TC9704**	**TD9805**		**TC9704**	
	dTpa N = 59	**dTpa N = 135**	**dTpa +Hep B N = 134**	**dTpa*** N = 390**	**Td N = 151[§]**
Local Reactions					
Redness	8.5	9.6	12.7	7.2	6.6
Swelling	18.6	15.6	20.1	11.3	13.9
Pain	94.9	69.6	75.4	84.6	86.1
Systemic Reactions					
Fever*	5.1	0.7	1.5	1.3	1.3
Headache	37.3	28.1	23.9	14.4	13.9
Chills	15.3	12.6	13.4	3.6	2.0
Body ache	15.3	18.5	19.4	11.8	8.6
Tiredness	23.7	37.0	31.3	11.5	14.6
Sore Joints	3.4	19.3	12.7	5.4	4.0
Nausea	6.8	12.6	12.7	6.9	5.3
Vomiting	1.7	0.0	1.5	0.5	0.0
Diarrhoea	1.7	4.4	3.0	2.3	1.3

* Includes fever ≥37.5°C and ≥ 39.1°C

** 12 - 18 years of age in TC9704 and 11-12 years of age in TD9805

*** >19 years of age

§ Includes (N=20) adolescents

Post-marketing Experienee

In addition to the data from clinical studies, the following adverse events have been reported during the commercial use of ADACEL. All the adverse events have been very rarely reported (<0.01%); however, the exact incidence rates cannot precisely be calculated. This computation is based on the number of adverse events reported per estimated number of vaccinated patients.

Immune System Disorders:

Hypersensitivity (anaphylactic) reaction (angioedema, oedema, rash, hypotension)

Nervous System Disorders:

Paraesthesia, hypoesthesia, Guillain-Barré syndrome, brachial neuritis, facial palsy, convulsion, syncope, myelitis

Metabolism and Nutrition Disorders:

Anorexia

Cardiac Disorders:

Myocarditis

Skin and Subcutaneous Tissue Disorders:

Pruritus, urticaria

Musculoskeletal and Connective Tissue Disorders:

Myositis, myalgia

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 occur 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.

Injection site bruising, sterile abscess

Underarm lymph node swelling

Potential Adverse Events

Other adverse events not listed above have been reported with other similar vaccines and should be considered potential adverse reactions to ADACEL. Although rarely, severe local reactions such as whole arm swelling following adsorbed tetanus vaccine has occurred and may be associated with high levels of antitoxin resulting from over-immunisation.

In addition, neurological conditions including peripheral neuropathies and demyelinating diseases of the central nervous system have been reported in temporal association with some tetanus or tetanus and diphtheria toxoid-containing vaccines.

Clinical data for use of ADACEL in individuals who have only received DTaP vaccines for priming in infancy and early childhood are currently not available.

Very rarely, large local reactions, consisting of redness and/or swelling > 50mm, some with circumferential swelling of the injected limb, have been reported following the fourth and fifth paediatric doses of some acelluar pertussis-containing vaccine.

DOSAGE AND ADMINISTRATION

The same dosage, a single 0.5 mL dose, applies to all age groups.

Booster doses of ADACEL should be given according to State and Federal recommendations.

Individuals with an incomplete, or no, history of a primary series of diphtheria and tetanus toxoids should not be vaccinated with ADACEL. A booster response will only be elicited in individuals who have been previously primed by vaccination.

The current Australian Immunisation Handbook recommends a booster dose of dTpa for the following groups, unless contraindicated (refer to CONTRAINDICATIONS);

- Adolescents at age of 15 to 17 years and again at 50 years.
- Before planning pregnancy, or for both parents as soon as possible after delivery of an infant.
- For adults working with young children, particularly for health-care workers and child-care workers in contact with the youngest infants such as maternity and nursery staff.
- Any adult expressing an interest in receiving a booster dose of dTpa should be encouraged to do so provided that primary course of DTP vaccine has been given in the past. With this same provision, dTpa can be used instead of adult diphtheria-tetanus vaccine as a booster for adults at 50 years.

The vaccine's normal appearance is a uniform, cloudy, white suspension which may sediment during storage. Shake the vial well to uniformly distribute the suspension before withdrawing the dose.

Parenteral biological products should be inspected visually for extraneous particulate matter and/or discolouration prior to administration. If these conditions exist, the product should not be administered.

When administering a dose from a stoppered vial, do not remove either the stopper or the metal seal holding it in place. Once the vial has been opened, any of its contents not used immediately should be discarded. Aseptic technique must be used for withdrawal of the dose. Before injection, the skin over the site should be cleansed with a suitable germicide.

ADACEL should be administered intramuscularly. The preferred site is into the deltoid muscle.

The intravascular or subcutaneous routes should not be used (for exception, see under PRECAUTION).

After insertion of the needle, ensure that the needle has not entered a blood vessel.

ADACEL must not be mixed in the same syringe with other vaccines or other parenterally administered drugs or co-administered in the same syringe.

Product is for single use in one patient on one occasion only. Discard any residue.

OVERDOSAGE

Not applicable

PRESENTATION AND STORAGE CONDITIONS

ADACEL is supplied as a single dose (0.5 mL) in a 2 mL glass vial.

Store at 2°C to 8°C. REFRIGERATE. DO NOT FREEZE. Do not use after expiry date.

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POISON SCHEDULE OF THE MEDICINE

S4 - Prescription Only Medicine

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS

21 November 2005

DATE OF MOST RECENT AMENDMENT

25 March 2013