AUSTRALIAN PRODUCT INFORMATION

NAME OF THE DRUG

ADACEL® POLIO

Pertussis Vaccine - Acellular and Diphtheria and Tetanus Toxoids (Adsorbed) Combined with Inactivated Poliovirus Type 1, 2 and 3 (Vero cell)

DESCRIPTION

ADACEL® POLIO is a sterile, uniform cloudy, white suspension for injection in prefilled syringes or vials.

Each 0.5 mL dose of ADACEL® POLIO 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[a])	tetanus toxoid
40 DagU	poliovirus inactivated type 1, Vero (Mahoney)
8 DagU	poliovirus inactivated type 2, Vero (MEF1)
32 DagU	poliovirus inactivated type 3, Vero (Saukett)
1.5 mg	aluminium phosphate (equivalent to 0.33 mg aluminium)
0.6% v/v	phenoxyethanol
≤0.025 µg	polymyxin B sulphate
≤0.02 µg	neomycin
≤0.2 µg	streptomycin
≤0.005 mg	formaldehyde
≤0.02 mg	glutaraldehyde
≤0.01%	polysorbate 80

water for injections to 0.5 mL

[a] The formulated content of 5LfU per 0.5 mL of tetanus toxoid is the same as in 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); and poliomyelitis viruses type 1, 2 and 3 cultivated on Vero cells, purified and then inactivated by formaldehyde.

ADACEL® POLIO is a diphtheria-tetanus-acellular pertussis combination vaccine (dTpa) combined with inactivated poliovirus vaccine with a reduced content of pertussis toxoid, filamentous haemagglutinin and diphtheria toxoid compared to paediatric diphtheria-tetanus-acellular pertussis (DTPa) formulations.

ADACEL® POLIO should not be used as part of a primary course of immunisation for diphtheria, tetanus, pertussis or poliomyelitis.

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

Immune responses of adults, adolescents and children 3 to 6 years of age one month after vaccination with ADACEL® POLIO are shown in Table 1 below.

Table 1: Immune Responses 4 Weeks After Vaccination

Antigen	Criteria	Adults and adolescents* (N = 986)	Children 5-6 years old† (N = 240)	Children 3-5 years old‡ (N = 148)
Seroprotection Rates				
Diphtheria (1)	≥0.1 IU/ mL	92.8%	99.4%§	100%
Tetanus (2)	≥0.1 IU/ mL**	100%	99.5%	100%
Polio 1	≥1:8 Dilution	99.9%	100%	100%
Polio 2	≥1:8 Dilution	100%	100%	100%
Polio 3	≥1:8 Dilution	100%	100%	100%
Seroconversion Rates				
Pertussis (3)				
PT	≥5 EU/mL††	99.7%	91.2%	99.3%
FHA	≥5 EU/mL††	99.9%	99.1%	99.3%
PRN	≥5 EU/mL††	99.6%	100%	100%
FIM	≥5 EU/mL††	99.8%	99.5%	100%
Pertussis				
PT	4-fold rise	84.0%	92.9%	92.6%
FHA	4-fold rise	78.4%	80.2%	91.2%
PRN	4-fold rise	95.1%	96.7%	96.0%
FIM	4-fold rise	88.9%	93.3%	86.5%

* From the age of 11 years onwards

† Primed with DTPa (Diphtheria toxoid (paediatric dose), tetanus toxoid and acellular pertussis vaccine) at 3 and 5 months with a booster at 12 months of age

‡ Primed with DTPw (Diphtheria toxoid (paediatric dose), tetanus toxoid and whole cell pertussis vaccine) at 2, 3 and 4 months of age

§ Tested by Vero Cell Neutralization Assay (n=162)

** Measured by ELISA

†† EU = ELISA units: Antibody levels of >5 EU/mL were postulated as surrogate markers for protection against pertussis.

The safety and immunogenicity profile of ADACEL® POLIO in adults and adolescents was shown to be comparable to that observed with a single booster dose of an adult formulation diphtheria-tetanus (Td), aP or Td Polio adsorbed vaccines containing the same amount of tetanus and diphtheria toxoids, pertussis antigens and inactivated poliovirus types 1, 2 and 3 administered separately.

The lower response to diphtheria toxoid in adults probably reflected the inclusion of some participants with an uncertain or incomplete immunisation history.

Serological correlates for protection against pertussis have not been established. On comparison with data from the two separate pertussis efficacy trials conducted in Sweden between 1992 and 1996, where primary immunisation with Sanofi Pasteur Limited's acellular pertussis infant DTPa formulations conferred a protective efficacy of 85% against pertussis disease, it was considered that ADACEL® POLIO had elicited protective immune responses.

Immune responses of children 4 to 6 years of age, primed with 4 doses of DTPa, one month after vaccination with ADACEL® are shown in Table 2 below.

Table 2: Immune Responses 4 Weeks After Vaccination With ADACEL® (dTpa)

Antigen	Criteria	Children 4-6 years old* (N =265)
Seroprotection Rates		
Diphtheria (1)	≥0.1 IU/ mL	100%
Tetanus (2)	≥0.1 IU/ mL†	100%
Seroconversion Rates		
Pertussis (3)		
PT	≥5 EU/mL‡	99.6
FHA	≥5 EU/mL‡	99.6
PRN	≥5 EU/mL‡	100.0
FIM	≥5 EU/mL‡	100.0
Pertussis		
PT	4-fold rise	91.9%
FHA	4-fold rise	88.1%
PRN	4-fold rise	94.3%
FIM	4-fold rise	94.6%

* Primed with DTPa at 2, 4 and 6 months and with a booster at 18 months of age.

† Measured by ELISA.

‡ EU = ELISA units: Antibody levels of >5 EU/mL were postulated as surrogate markers for protection against pertussis.

Seroprotection rates 3 years post-vaccination with ADACEL® POLIO in adults and adolescents are shown in Table 3 below.

Table 3: Seroprotection Rates 3 Years Post-Vaccination with ADACEL® POLIO in Adults and Adolescents

Antigen	Criteria	Adults and adolescents* (N = 251)
Seroprotection Rates		
Diphtheria (1)	≥0.01 IU/mL	95.6%
Tetanus (2)	≥0.01 IU/mL†	100%
Polio 1	≥1:8 Dilution	100%
Polio 2	≥1:8 Dilution	100%
Polio 3	≥1:8 Dilution	100%
Seroconversion Rates		
Pertussis (3)		
PT	≥5 EU/mL‡	96.8%
FHA	≥5 EU/mL‡	100.0%
PRN	≥5 EU/mL‡	100.0%
FIM	≥5 EU/mL‡	98.0%

* From the age of 11 years onwards.

† Measured by ELISA.

‡ EU = ELISA units: Antibody levels of >5 EU/mL were postulated as surrogate markers for protection against pertussis.

There are currently no data available on the antibody levels to any of the antigens in ADACEL® POLIO beyond four weeks post-vaccination in children.

INDICATIONS

ADACEL® POLIO is indicated for active immunisation against diphtheria, tetanus, pertussis and poliomyelitis in adults, adolescents and children aged 4 years and older as a booster following primary immunisation.

Children 4-6 years of age should have already received four doses of DTPa and IPV or OPV.

ADACEL® POLIO is not intended for primary immunisation.

The use of ADACEL® POLIO should be determined on the basis of official recommendations.

CONTRAINDICATIONS

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

ADACEL® POLIO 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, glutaraldehyde, streptomycin, neomycin and polymyxin B).

ADACEL® POLIO 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® POLIO.

WARNINGS

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, such as whether or not the primary immunisation schedule has been completed. Vaccination is usually justified for infants whose primary immunisation schedules are incomplete (i.e., fewer than three doses have been received).

PRECAUTIONS

The use of ADACEL® POLIO 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 or by natural infection.

To minimise the risk of adverse reactions, ADACEL® POLIO should not be given to adults and adolescents who have received another vaccine containing either diphtheria or tetanus within the previous three years.

An acceptable safety profile was observed following administration of ADACEL® POLIO given as soon as 4 months after a diphtheria-containing vaccine (Meningococcal C conjugate vaccine (CRM_{197}) and 3 years after Diphtheria toxoid (paediatric dose), tetanus toxoid and pertussis vaccine (DTPw vaccine).

There are currently no data upon which to base a recommendation for the optimal interval for administering subsequent booster doses with ADACEL® POLIO to maintain antibody levels against pertussis.

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 the 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 increased 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, such as thrombocytopaenia, because of the risk of haemorrhage. In these situations administration of ADACEL® POLIO by deep subcutaneous injection may be considered, although there is a risk of increased local reactions.

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

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® POLIO 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 a mild upper respiratory infection, is not usually a reason to defer immunisation.

Carcinogenicity, mutagenicity, impairment of fertility

ADACEL® POLIO has not been evaluated for carcinogenicity, mutagenicity or impairment of fertility.

Use in pregnancy (Category B2)

The effect of ADACEL® POLIO 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® POLIO 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® POLIO during lactation has not been assessed. As ADACEL® POLIO is detoxified, any risk to the mother or the infant is improbable. The benefits versus the risks of administering ADACEL® POLIO 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.

Use in children

ADACEL® POLIO should not be used for primary immunisation.

ADACEL® POLIO is indicated for use in children aged four years and older.

INTERACTIONS

A clinical study has shown that ADACEL® POLIO can be safely administered concomitantly with hepatitis B vaccine, using a separate limb for the site of injection. ADACEL® POLIO has safely been given concomitantly with measles-mumps-rubella vaccine (MMR™ II). Interaction studies have not been carried out with other vaccines, biological products or therapeutic medications. However, in accordance with commonly accepted immunisation guidelines, since ADACEL® POLIO is an inactivated product, there is no theoretical reason why it should not be administered concomitantly with other vaccines or immunoglobulins at separate sites.

In the case of immunosuppressive therapy, refer to PRECAUTIONS.

ADVERSE REACTIONS

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

Adolescents and Adults (992 subjects)

In clinical studies in which ADACEL® POLIO was administered to adolescents and adults, the most frequently reported adverse reactions occurring over all age groups during the first 24 hours after vaccination included the following:

Very common:	Injection site pain, erythema and swelling, tiredness, headache, bodyache, chills, nausea, fever, arthralgia or joint swelling
Common:	Diarrhoea, vomiting

There was a trend for higher rates of local and systemic reactions in adolescents than in adults. In both age groups, injection site pain was the most common adverse reaction.

Late-onset local adverse reactions (i.e. a local adverse reaction which had an onset or increase in severity 3 to 14 days post-immunisation), such as injection site pain, erythema and swelling, occurred in less than 1.2%.

Table 4 summarises adverse events (%) in ADACEL® POLIO (dTpa-IPV) recipients 0 - 24 hours post vaccination:

Table 4: Adverse Events (%) in ADACEL® POLIO (dTpa-IPV) recipients 0 - 24 hours post vaccination

Event	Children*	Adolescents†		Adults ‡	
	Sweden 5.5 Yr	TD9707	TD9809	TD9707	
	dTpa-IPV (N = 240)	dTpa-IPV (N = 350)	dTpa-IPV§ (N =144)	dTpa-IPV (N = 366)	dT (N = 126)
Local Reactions	%	%	%	%	%
Redness (Any)	-	13.5	25.0	19.7	19.8
Redness (≥2 cm)	7.5	-	-	-	-
Redness (≥5 cm)	3.3	-	-	-	-
Swelling (Any)	-	16.4	21.5	14.2	7.2
Swelling (≥2 cm)	11.7	-	-	-	-
Swelling (≥5 cm)	3.3	-	-	-	-
Pain	60.8	87.9	95.8	84.4	82.5
Systemic Reactions	%	%	%	%	%
Fever**	9.7	10.8	2.1	1.4	0.0
Headache	-	26.4	35.4	15.0	13.5
Chills	-	13.8	17.4	3.8	3.2
Body ache	-	19.8	41.0	13.4	11.9
Tiredness	11.7	29.9	40.3	15.6	16.7
Sore/Swollen Joints	-	9.2	18.1	4.1	4.8
Nausea	-	10.6	13.9	6.8	5.6
Vomiting	0.4	1.2	1.4	0.3	0.8
Diarrhoea	0.4	1.2	2.1	3.6	2.4

* ≥5 to <6 years in Swedish children; these children were primed with DTPa at 3, 5 and 12 months of age.

† ≥12 to <19 years of age in TD9707, and ≥11 to <14 years of age in TD9809

‡ ≥19 to 60 years of age

§ The rates for dTpa-IPV administered alone or concomitantly with Hepatitis B vaccine were comparable.

** Includes fever ≥38.0°C.

Children 3 to 5 years old (150 subjects)

In two clinical studies (U01-Td5I-303 and U01-Td5I-402) 150 children primed at 2, 3 and 4 months of age with a DTPw vaccine (with no additional dose in the second year of life) received ADACEL® POLIO at 3 to 5 years of age. The most frequently reported adverse reactions occurring during the first 7 days included the following:

Very common:	Injection site pain, erythema and swelling; fatigue, fever ≥37.5°C, irritability
Common:	Injection site bruising and dermatitis; diarrhoea, vomiting and rash

Children 5 to 6 years old (240 subjects)

In a clinical study, children were primed at 3, 5 and 12 months of age with a DTPa vaccine with no additional dose in the second year of life. These children received ADACEL® POLIO at 5 to 6 years of age. The most frequently reported adverse reactions occurring during the first 24 hours included the following:

Very common:	Injection site pain and swelling; fatigue
Common:	Injection site erythema and pruritus; fever ≥38°C
Uncommon:	Diarrhoea, vomiting

The rates of general symptoms after the first day but within 10 days after vaccination were low; only fever (≥38°C) and fatigue were reported in >10% of subjects. Transient severe swelling of the upper arm was reported in <1% of subjects.

Children 4 to 6 years old (298 subjects)

In a clinical study, children primed with DTPa at 2, 4 and 6 months and a booster at 18 months of age received ADACEL® (dTpa) at 4 to 6 years of age. The most frequently reported adverse reaction that occurred during the first 3 days was pain at 38.3%. Erythema and swelling were also commonly reported.

Post-Marketing Experience

Based on spontaneous reporting, the following additional adverse events have been reported very rarely (<1/10,000) during the postmarketing surveillance of dTpa-IPV. Their frequencies have been estimated using number of reports and estimated number of patients. However, exact incidence cannot be precisely calculated.

Blood and lymphatic disorders:

Lymphadenopathy

General disorders and administration site conditions:

Malaise, Pallor

Extensive limb swelling, which may extend from the injection site beyond one or both joints and is frequently associated with erythema and sometimes with blisters, have been reported following administration of dTpa-IPV. The majority of these reactions appeared within 48 hours of vaccination and spontaneously resolved over an average of 4 days without sequelae. The risk appears to be dependent of the number of prior doses of DTPa vaccine, with a greater risk following the 4^{th} and 5^{th} doses.

Immune system disorders:

Anaphylactic reactions, such as urticaria, face oedema and dyspnoea.

Potential Adverse Events

Brachial neuritis and Guillain-Barré syndrome after administration of a tetanus toxoid containing vaccine.

DOSAGE AND ADMINISTRATION

The same dosage, a single 0.5 mL dose, applies to all age groups. ADACEL® POLIO may be administered from the age of four years onwards.

ADACEL® POLIO should be administered in accordance with current NHMRC recommendations. (4)

The Australian Immunisation Handbook (4) 2003 recommends a booster dose with a vaccine containing an adult formulation tetanus-diphtheria-acellular pertussis (dTpa) for the following groups, unless contraindicated. (Refer to CONTRAINDICATIONS.);

- Adolescents at 15 to 17 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 particular 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 DTPa 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.

In addition, a booster dose for poliomyelitis is recommended for the following:

- Children at 4 years of age;
- Travellers to areas or countries where poliomyelitis is epidemic or endemic;
- Health-care workers in possible contact with poliomyelitis cases.

ADACEL® POLIO has not been studied in subjects with tetanus prone injuries and should not be used in these circumstances.

Method of administration

The vaccine's normal appearance is a cloudy, white suspension, which may sediment during storage. Shake the vial, or the prefilled syringe, well to distribute uniformly the suspension before administering the vaccine.

Parenteral biological products should be inspected visually for extraneous particulate matter and/or discolouration prior to administration. In the event of either being observed, discard the vaccine.

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

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

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

ADACEL® POLIO 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

ADACEL® POLIO is supplied in a prefilled syringe or vial for single dose (0.5 mL) use.

STORAGE

Store at 2° 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 ARTG

06 June 2006

DATE OF MOST RECENT AMENDMENT

15 October 2012

References List

1 Galazka AM. Module 2: Diphtheria. In: The immunological basis for immunization series. WHO/EPI/GEN/93.12 Geneva: World Health Organization; 1993.

2 Galazka AM. Module 3: Tetanus. In: The immunological basis for immunization series. WHO/EPI/GEN/93.13 Geneva: World Health Organization; 1993.

3 Storsaeter J. et al, Levels of anti-pertussis antibodies related to protection after household exposure to Bordetella pertussis. Vaccine 1998;16(20):1907-16.

4 The Australian Immunisation Handbook 8th Edition 2003. National Health and Medical Research Council (NHMRC) p. 210-11.