

# DATA SHEET

## Name of the Medicinal Product

### INFANRIX

*Combined diphtheria, tetanus, acellular pertussis vaccine*

## Presentation

INFANRIX is presented as a turbid white suspension in a glass prefilled syringe. Upon storage a white deposit and clear supernatant is observed.

INFANRIX contains diphtheria toxoid, tetanus toxoid and three purified pertussis antigens [pertussis toxoid (PT), filamentous haemagglutinin (FHA) and 69 kilodalton (kDa) outer membrane protein (pertactin)] adsorbed onto aluminium salts.

The diphtheria and tetanus toxins are obtained from cultures of *Corynebacterium diphtheriae* and *Clostridium tetani* and are then detoxified and purified. The acellular pertussis vaccine components (PT, FHA and pertactin) are prepared by growing phase I *Bordetella pertussis* from which the PT and FHA and pertactin are extracted, purified and treated with formaldehyde; PT is irreversibly detoxified.

The diphtheria toxoid, tetanus toxoid and acellular pertussis vaccine components are adsorbed on aluminium salts. The final vaccine is formulated in saline and contains 2-phenoxyethanol as preservative.

INFANRIX meets the World Health Organisation requirements for biological substances and for diphtheria and tetanus vaccines. No substances of human origin are used in its manufacture.

A 0.5mL dose of the vaccine contains not less than 30 International Units (IU) of diphtheria toxoid, 40 IU of tetanus toxoid, 25 µg of PT, 25 µg of FHA and 8 µg of pertactin.

## Clinical Particulars

### ***Therapeutic indications***

INFANRIX (DTPa) is indicated for active primary immunisation against diphtheria, tetanus and pertussis.

INFANRIX is indicated as fourth and/or fifth dose for children from 15 months of age up to and including 6 years of age who have previously been immunised with three or four doses of diphtheria, tetanus and pertussis (whole cell or acellular) vaccine.

### ***Posology and method of administration***

INFANRIX is administered by intramuscular injection. THE VACCINE SHOULD NEVER BE ADMINISTERED INTRAVENOUSLY.

The recommended dose (0.5 mL) of the vaccine must be administered.

The primary immunisation course consists of 3 doses with boosters during the second and sixth year of life.

Each dose consists of a 0.5mL ready to use sterile suspension. Before use of INFANRIX, the vaccine should be well shaken to obtain a homogenous turbid suspension. Discard the vaccine if it appears otherwise.

All parenteral drug and vaccine products should be inspected visually for any particulate matter or discolouration prior to administration.

INFANRIX should be injected intramuscularly in the lateral aspect of the thigh or the deltoid region of the arm.

### ***Contraindications***

INFANRIX should not be administered to subjects with known hypersensitivity to any component of the vaccine or to subjects having shown signs of hypersensitivity after previous administration of INFANRIX, diphtheria and tetanus vaccine and DTPw.

INFANRIX is contraindicated if the child has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis containing vaccine. In these circumstances the vaccination course should be continued with diphtheria and tetanus vaccine.

### ***Special warnings and special precautions for use***

It is good clinical practice that immunisation should be preceded by a review of the medical history (especially with regard to previous immunisation and possible occurrence of undesirable events) and a clinical examination.

As with other vaccines, the administration of INFANRIX should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection, however, is not a contraindication.

If any of the following events occur in temporal relation to receipt of DTPa or DTPw, the decision to give subsequent doses of vaccine containing the pertussis component should be carefully considered. There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks, particularly since these events are not associated with permanent sequelae.

The following events were previously considered contra-indications for DTPw and can now be considered general precautions :

- Temperature of > 40.5°C within 48 hours of vaccination, not due to another identifiable cause.
- Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours of vaccination.
- Persistent, inconsolable crying lasting > 3 hours, occurring within 48 hours of vaccination.
- Convulsions with or without fever, occurring within 3 days of vaccination.

A history of febrile convulsions and a family history of convulsive fits do not constitute contraindications.

HIV infection is not considered as a contraindication. However in patients with immunodeficiency or in patients receiving immunosuppressive therapy, an adequate immunologic response may not be achieved.

As with all injectable vaccines, appropriate medical treatment should always be readily available in case of anaphylactic reactions following the administration of the vaccine. For this reason, the vaccinee should remain under medical supervision for 30 minutes after immunisation.

As for all diphtheria, tetanus and pertussis vaccines, the vaccine should be given deep intramuscularly and preferably at alternate injection sites.

INFANRIX should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects.

INFANRIX should under no circumstances be administered intravenously.

#### ***Interaction with other medicinal products and other forms of interaction***

INFANRIX can be administered in any temporal relationship with other childhood vaccines.

Different injectable vaccines should always be administered at different injection sites.

INFANRIX must not be mixed with other vaccines.

#### ***Use during pregnancy and lactation***

As INFANRIX is not intended for use in adults, adequate human data on use during pregnancy or lactation and adequate animal reproduction studies are not available.

#### ***Effects on ability to drive and use machines***

Not applicable.

#### ***Undesirable effects***

In controlled clinical studies, signs and symptoms were actively monitored and recorded on diary cards in all vaccinees following the administration of each dose of the vaccine.

The following table, based on the results of comparative studies summarises the local solicited symptoms reported within 48 hours of vaccination as a percentage of doses administered.

Local solicited symptoms	Primary immunisation		Booster			
	Infanrix (1275)	DTPw (455)	Infanrix after	DTPw after	Infanrix after	DTPw after

	doses)	doses)	Infanrix primary (269 doses)	DTPw primary (92 doses)	DTPw primary (273 doses)	DTPw primary (91 doses)
pain	2.5	19.1	15.6	55.4	15.8	59.3
redness (> 2 cm)	0.1	1.1	4.5	3.3	2.2	5.5
swelling (> 2 cm)	0	1.3	3.0	7.6	1.5	5.5

General solicited symptoms which were reported in the same comparative studies and within the same timeframe are summarised in the following table.

General solicited symptoms (%)	Primary immunisation		Booster			
	Infanrix	DTPw	Infanrix after Infanrix primary	DTPw after DTPw primary	Infanrix after DTPw primary	DTPw after DTPw primary
fever > 38 °C (rectal)	9.9	42.2	26.8	64.1	29.3	63.7
fever > 39.5 °C (rectal)	0.2	1.3	0.4	4.3	0.7	4.4
unusual crying	5.2	11.9	8.6	14.7	2.6	11.0
vomiting	3.0	4.4	3.3	7.6	2.6	2.2
diarrhoea	5.9	6.8	11.2	13.0	8.1	16.5
eating and drinking less than usual	4.2	20.7	7.1	43.5	12.5	29.7
sleeping more than usual / drowsiness	9.3	13.6	10.4	31.5	10.3	14.3
sleeping less than usual / restlessness	9.3	16.7	12.3	32.6	7.7	16.5

Additional safety data are available from other studies, which evaluate the primary immunisation course and the booster dose administration. These studies, which include non-comparative studies, confirmed the safety profile of DTPa which is summarised above. Redness and swelling of more than 10 cm have been reported after the booster dose and these resolved spontaneously. As with other vaccines such as DT and DTP, swelling of the entire thigh has occasionally been observed.

The following unsolicited symptoms have been reported for

- INFANRIX primary immunisation:  
Skin and appendages (1% or less): dermatitis  
Respiratory system (3% or less): coughing, rhinitis, bronchitis, other upper respiratory tract infection  
Resistance mechanism (1% or less): otitis media
- INFANRIX booster following INFANRIX primary immunisation (total of 2363 documented doses):  
Respiratory system (4% or less): coughing, pharyngitis, bronchitis, other upper

respiratory tract infection, rhinitis, respiratory disorder

Resistance mechanism (3% or less): viral infection, otitis media

- INFANRIX booster following DTPw primary immunisation (total of 606 documented doses):

Respiratory system (3% or less): coughing, pharyngitis, upper respiratory tract infection, bronchitis.

Resistance mechanism (2% or less): otitis media.

Extremely rare cases of collapse or shock-like state (hypotonic-hyporesponsiveness episode) and convulsions within 2 to 3 days of vaccination have been reported. All the subjects recovered totally and spontaneously without sequelae.

Very rare allergic reactions, including anaphylactoid reactions, have been reported.

### **Overdose**

Not applicable.

## **Pharmacological Properties**

### ***Pharmacodynamic properties***

#### **Immune response of INFANRIX primary immunisation**

One month after a three-dose primary vaccination course in the first 6 months of life more than 99% of infants vaccinated with INFANRIX had antibody titers of more than 0.1 IU/ml to both diphtheria and tetanus.

The vaccine contains PT, FHA and pertactin, antigens which are considered to play an important role in protection against pertussis disease. In clinical studies, the vaccine response to these pertussis antigens was more than 95%.

#### **Immune response of INFANRIX booster immunisation**

Following administration of an INFANRIX booster in the second year of life (13-24 months) all INFANRIX-primed infants had antibody titers of more than 0.1 IU/ml to both diphtheria and tetanus.

The booster response to the pertussis antigens was seen in more than 96% of these children.

### **Protective efficacy of INFANRIX**

The protective efficacy of INFANRIX against WHO-defined typical pertussis (21 days of paroxysmal cough with laboratory confirmation) was demonstrated in :

- A prospective blinded household contact study performed in Germany (3, 4, 5 months schedule).  
Based on data collected from secondary contacts in households where there was an index case with typical pertussis, the protective efficacy of the vaccine was 88.7%.  
Protection against laboratory confirmed mild disease, defined as 14 days or more of cough of any type was 73% and 67% when defined as 7 days or more of cough of any type.

- An NIH sponsored efficacy study performed in Italy (2, 4, 6 months schedule). The vaccine efficacy was found to be 84%. When the definition of pertussis was expanded to include clinically milder cases with respect to type and duration of cough, the efficacy of INFANRIX was calculated to be 71% against >7 days of any cough and 73% against >14 days of any cough.

### ***Pharmacokinetic properties***

Evaluation of pharmacokinetic properties is not required for vaccines.

### ***Preclinical safety data***

Appropriate safety tests have been performed.

## **Pharmaceutical Particulars**

### **Special precautions for storage**

INFANRIX should be stored between +2°C and +8°C. DO NOT FREEZE, discard if vaccine has been frozen.

### **Shelf life**

The expiry date of the vaccine is indicated on the label and packaging. The shelf life of INFANRIX is 36 months from the date of manufacture at a temperature of +2°C to +8°C.

## **Medicine Classification**

Prescription Medicine

## **Package Quantities**

Prefilled syringes: 0.5mL in packs of 1.

## **Name and Address**

GlaxoSmithKline NZ Ltd  
Quay Tower  
Cnr Albert & Customs Street  
Private Bag 106600  
Downtown  
Auckland  
NEW ZEALAND

ph (09) 367 2900

fax (09) 367 2506

## **Date of Preparation**

23 October 2002

Version 2.0