

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

INFANRIX diphtheria-tetanus-acellular pertussis (DTPa) vaccine suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

INFANRIX contains diphtheria toxoid, tetanus toxoid and three purified pertussis antigens [pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN)] adsorbed onto aluminium salts.

A 0.5 mL dose of the vaccine contains:

Diphtheria toxoid not less than 30 International Units (IU)

Tetanus toxoid not less than 40 International Units (IU)

Bordetella pertussis antigens

Pertussis toxoid (PT) 25 micrograms (μg)

Pertussis Filamentous Haemagglutinin (FHA) 25 micrograms (μg)

Pertactin (PRN) (69 kiloDalton (kDa) outer membrane protein) 8 micrograms (μg)

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 PRN) are prepared by growing phase I *Bordetella pertussis* from which the PT and FHA and PRN 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.

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

For the full list of excipients, see section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

Suspension for injection.

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

4. CLINICAL PARTICULARS

4.1 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.

4.2 Dose and method of administration

Dose

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 0.5 mL 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 (see section 6.6 Special precautions for disposal and other handling).

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

Method of administration

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

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

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: following injection, firm pressure should be applied to the injection site (without rubbing) for at least two minutes.

4.3 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.

4.4 Special warnings and 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 $\geq 40.5^{\circ}\text{C}$ 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.

In children with progressive neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy, it is better to defer pertussis (Pa or Pw) immunisation until the condition is corrected or stable. However, the decision to give pertussis vaccine must be made on an individual basis after careful consideration of the risks and benefits.

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.

The potential risk of apnoea and the need for respiratory monitoring for 48-72 hours should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

4.5 Interaction with other medicines and other forms of interaction

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

INFANRIX can be mixed in the same syringe with HIBERIX or Act-HIB. Different injectable vaccines should always be administered at different injection sites.

INFANRIX should not be mixed with other vaccines, with the exception of those mentioned above.

In patients receiving immunosuppressive therapy or patients with immunodeficiency an adequate immunologic response may not be achieved.

4.6 Fertility, 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.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Tabulated list of adverse reactions

Clinical trial data

The safety profile presented below is based on data from more than 11400 subjects.

As has been observed for DTPa and DTPa-containing combinations, an increase in local reactogenicity and fever was reported after booster vaccination with INFANRIX with respect to the primary course.

Adverse reactions reported are listed according to the following frequencies:

Very common: $\geq 1/10$

Common: $\geq 1/100$ to $<1/10$

Uncommon: $\geq 1/1,000$ to $<1/100$

Rare: $\geq 1/10,000$ to $1/1,000$

Very rare: $< 1/10,000$

Blood and lymphatic system disorders

Very rare: Lymphadenopathy¹

Metabolism and nutrition disorders

Common: appetite lost²

Psychiatric disorders:

Very common: irritability

Common: restlessness², crying abnormal

Nervous system disorders:

Very common: somnolence

Uncommon: headache¹

Respiratory, thoracic and mediastinal disorders:

Uncommon: cough¹, bronchitis¹

Gastrointestinal disorders:

Common: gastrointestinal disorders such as diarrhoea and vomiting

Skin and subcutaneous tissue disorders:

Common: pruritus

Uncommon: rash

Rare: urticaria

General disorders and administration site conditions:

Very common: redness, local swelling at the injection site (≤ 50 mm), fever $\geq 38.0^{\circ}\text{C}$,

Common: pain², local swelling at the injection site (>50 mm)³

Uncommon: injection site reactions including indurations, fatigue¹, fever $\geq 39.1^{\circ}\text{C}$, diffuse swelling of the injected limb, sometimes involving the adjacent joint. ³

Post-marketing data**Blood and lymphatic system disorders:**

Thrombocytopenia⁴

Immune system disorders:

Allergic reactions, including anaphylactic and anaphylactoid reactions

Nervous system disorders:

Collapse or shock-like state (hypotonic-hyporesponsiveness episode), convulsions (with or without fever) within 2 to 3 days of vaccination

Respiratory, thoracic and mediastinal disorders:

Apnoea [see section 4.4 Special warnings and precautions for use for apnoea in very premature infants (≤ 28 weeks of gestation)]

Skin and subcutaneous tissue disorders:

Angioneurotic oedema

General disorders and administration site conditions:

Swelling of the entire injected limb³

¹ Reported only with booster vaccination

² Very common for booster vaccination

³ Children primed with acellular pertussis vaccines are more likely to experience swelling reactions after booster administration in comparison with children primed with whole cell vaccines. Local swelling at the injection site (>50 mm) and diffuse swelling may be more frequent (very common and common, respectively) when the booster dose is administered between 4 and 6 years. These reactions resolve over an average of 4 days.

⁴ Reported with D and T vaccines.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions via: <https://nzphvc.otago.ac.nz/reporting>.

4.9 Overdose

Cases of overdose have been reported during post-marketing surveillance. Adverse events, when reported, are not specific but similar to adverse events reported with normal vaccine administration.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Bacterial vaccines, ATC code J07AJ52.

Mechanism of Action

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 PRN, 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.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Appropriate safety tests have been performed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminium hydroxide, sodium chloride, water for injection.

Residues:

Polysorbate 80, formaldehyde.

6.2 Incompatibilities

INFANRIX should not be mixed with other vaccines in the same syringe, with the exception of HIBERIX or Act-HIB.

6.3 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.

6.4 Special precautions for storage

INFANRIX should be stored between +2°C and +8°C.

DO NOT FREEZE. Discard if the vaccine has been frozen.

6.5 Nature and contents of container

Prefilled syringes: 0.5 mL in packs of 1 and 10.

The prefilled syringes are made of neutral glass type I.

Not all pack sizes may be distributed in New Zealand.

6.6 Special precautions for disposal and other handling

Instructions for Handling

The vaccine should be shaken in order to obtain a homogenous turbid suspension and inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine.

As stated in section 4.5 Interaction with other medicines and other forms of interaction, INFANRIX can be mixed in the same syringe with HIBERIX or Act-HIB. In this case, the diluent supplied in the HIBERIX or Act-HIB package is replaced by INFANRIX.

From the HIBERIX or Act-HIB package, discard the vial containing the diluent. The combined vaccine must be reconstituted by adding the entire contents of the INFANRIX container to the vial containing the lyophilised powder.

The extemporaneous mix should be handled in the same way as the INFANRIX vaccine.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

GlaxoSmithKline NZ Limited
Private Bag 106600
Downtown
Auckland
NEW ZEALAND

Phone: (09) 367 2900

Facsimile: (09) 367 2910

9. DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine: 28 November 1996

10. DATE OF REVISION OF THE TEXT

1 June 2018

Summary table of changes:

| Section changed | Summary of new information |
|-----------------|---|
| All | Data Sheet re-format |
| 3 | Included pharmaceutical form |
| 4.5 | Clarification of information regarding mixing of INFANRIX with other vaccines |
| 4.8 | Updated definitions of adverse reaction frequencies |
| 4.8 | Added information on reporting of suspected adverse reactions |
| 4.9 | Added mandatory statement regarding overdose management |
| 6.2 | Clarification of information regarding mixing of INFANRIX with other vaccines |
| 6.6 | Clarification of information regarding mixing of INFANRIX with other vaccines |
| 6.6 | Added statement regarding the disposal of unused medicine or waste material |
| 9 | Added date of first approval |
| End of document | Updated trade mark and copyright statements |
| All | Minor editorial updates |

Version 5.0

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