NEW ZEALAND DATA SHEET

1. PRODUCT NAME

INFANRIX-IPV Combined diphtheria-tetanus-acellular pertussis (DTPa) and enhanced inactivated polio suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 dose (0.5 mL) contains:

Diphtheria toxoid[1]	not less than 30 International Units (IU) (25 Lf)
Tetanus toxoid[1]	not less than 40 International Units (IU) (10 Lf)
Bordetella pertussis antigens	
Pertussis toxoid (PT)[1]	25 micrograms
Filamentous Haemagglutinin (FHA)[1]	25 micrograms
Pertactin (PRN)[1]	8 micrograms
Poliovirus (inactivated) (IPV)	
type 1 (Mahoney strain)[2]	40 D-antigen unit
type 2 (MEF-1 strain)[2]	8 D-antigen unit
type 3 (Saukett strain)[2]	32 D-antigen unit

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.5 milligrams Al^{3+}

[2]propagated in VERO cells

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

3. PHARMACEUTICAL FORM

INFANRIX-IPV is a sterile, turbid white suspension for injection.

Upon storage, a white deposit and clear supernatant can be observed. This is not a sign of deterioration.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

INFANRIX-IPV is indicated for active primary immunisation in infants from the age of 2 months against diphtheria, tetanus, pertussis, and poliomyelitis.

INFANRIX-IPV is also indicated as a booster dose for children up to 13 years of age who have previously been immunised with diphtheria, tetanus, pertussis (DTP) and polio antigens.

4.2 Dose and method of administration

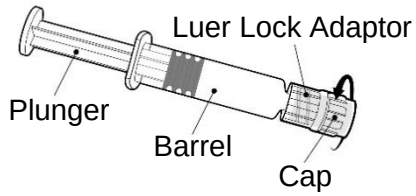
Dose

The primary vaccination schedule consists of three doses in the first year of life. An interval of at least 1 month should be respected between doses.

In order to maintain protection a booster dose is recommended. An interval of at least 6 months after completion of primary vaccination schedule should be adhered to. Local immunisation schedule recommendations should be followed for primary and booster doses.

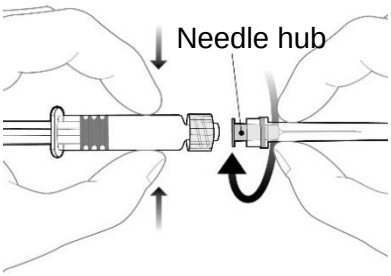
Data on the use of the vaccine as a booster has been obtained for children up to 13 years of age.

Instructions for the pre-filled syringe



Hold the syringe by the barrel, not by the plunger.

Unscrew the syringe cap by twisting it anticlockwise.



To attach the needle, connect the hub to the Luer Lock Adaptor and rotate a quarter turn clockwise until you feel it lock.

Do not pull the syringe plunger out of the barrel. If it happens, do not administer the vaccine.

Method of administration

INFANRIX-IPV is for deep intramuscular injection. For infants, the preferred site is the anterolateral aspect of the thigh; in older children, vaccine should be administered in the deltoid.

It is preferable that each subsequent dose is given at alternate sites.

INFANRIX-IPV should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects. Firm pressure should be applied to the injection site (without rubbing) for at least two minutes.

4.3 Contraindications

INFANRIX-IPV 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 diphtheria, tetanus, pertussis, or inactivated poliomyelitis vaccines.

INFANRIX-IPV is contraindicated if the child has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis containing vaccine.

4.4 Special warnings and precautions for use

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

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

If any of the following events occur in temporal relation to receipt of DTP-containing vaccine, 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 the events are not associated with permanent sequelae. According to available clinical data, the risk benefit ratio of acellular pertussis vaccine is better than the risk benefit ratio of whole cell pertussis vaccine. The following events were previously considered contra-indications for DTPw and can now be considered precautions:

- Temperature of $\geq$ 40.0 °C (rectal) within 48 hours, not due to another identifiable cause
- Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours of vaccination
- Persistent, inconsolable crying lasting $\geq$ 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, a family history of convulsions, a family history of Sudden Infant Death Syndrome (SIDS) or a family history of an adverse event following DTP and/or IPV vaccination do not constitute contra-indications.

Human Immunodeficiency Virus (HIV) infection is not considered as a contraindication.

The expected immunological response may not be obtained after vaccination of immunosuppressed patients, e.g. patients on immunosuppressive therapy.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

INFANRIX-IPV contains traces of neomycin and polymyxin. The vaccine should be used with caution in patients with known hypersensitivity to one of these antibiotics.

As with all diphtheria, tetanus, and pertussis vaccines, the vaccine should be given deep intramuscularly.

INFANRIX-IPV 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-IPV should under no circumstances be administered intravenously.

The potential risk of apnoea and the need for respiratory monitoring for 48-72h 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

It is routine practice in paediatric vaccination to co-administer different vaccines during the same session, where injectable vaccines should always be given at different injection sites.

INFANRIX-IPV can be administered concomitantly with measles, mumps, rubella, varicella, hepatitis B, and *Haemophilus influenzae type b* vaccines.

As with other vaccines it may be expected that in patients receiving immunosuppressive therapy or patients with immunodeficiency, an adequate response may not be achieved.

4.6 Fertility, pregnancy and lactation

Pregnancy

Adequate human data on use during pregnancy and adequate animal reproduction studies are not available.

Breast-feeding

Adequate human data on use during lactation and adequate animal reproduction studies are not available.

Fertility

Not applicable.

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 2200 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-IPV with respect to the primary course.

Frequencies per dose are defined as follows:

Very common: ≥ 1/10

Common: ≥ 1/100 and < 1/10

Uncommon: ≥ 1/1,000 and < 1/100

Rare: ≥ 1/10,000 and < 1/1,000

Very rare: < 1/10,000

Blood and lymphatic system disorders

Rare: Lymphadenopathy[1]

Metabolism and nutrition disorders

Very common: appetite lost

Psychiatric disorders

Very common: restlessness, crying abnormal, irritability

Nervous system disorders

Very common: headache[1] (age range 6-13 years old), somnolence

Respiratory, thoracic and mediastinal disorders

Rare: bronchitis[2], cough[2]

Gastrointestinal disorders

Common: nausea[1], vomiting, diarrhoea

Skin and subcutaneous tissue disorders

Uncommon: dermatitis allergic

Rare: urticaria, rash[2,3]

General disorders and administration site conditions

Very common: injection site reactions such as pain, redness, local swelling at the injection site (≤50 mm), fever ≥ 38.0°C

Common: local swelling at the injection site (>50 mm)[4], asthenia, malaise[1], injection site reactions including induration

Uncommon: diffuse swelling of the injected limb, sometimes involving the adjacent joint[4], fever[5] (>39.5°C)

Post-marketing data

Blood and lymphatic system disorders

Thrombocytopenia[6]

Immune system disorders

Allergic reactions, including anaphylactic[2] 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 disorders

Apnoea[2] (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

Pruritus, angioneurotic oedema[2]

General disorders and administration site conditions

Swelling of the entire injected limb[4], injection site vesicles

[1]reported only with booster vaccination

[2]reported with GSK's DTPa containing vaccines

[3]uncommonly reported with booster vaccination

[4]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.

[5]commonly reported with booster vaccination

[6]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

Pharmacotherapeutic group: Bacterial and viral vaccines combined, ATC code: J07CA02.

Clinical efficacy and safety

Immune response to the DT components:

One month after a primary vaccination course more than 99% of infants vaccinated with INFANRIX-IPV had antibody titers of ≥ 0.1 IU/ml to both tetanus and diphtheria.

Following administration of a booster dose of INFANRIX-IPV, more than 99.5% of children had antibody titers of ≥ 0.1 IU/ml for both antigens.

Immune response to the Pa component:

One month after the 3-dose primary vaccination course with INFANRIX-IPV 100% of infants were seropositive for the three pertussis components (PT, FHA, pertactin), and the overall response rates for each of the three individual pertussis antigens were ≥ 94%.

A booster response was seen in the vast majority of vaccinees against the pertussis antigens; lower response rates were seen in studies where the pre-vaccination levels of antibodies were high. All subjects were seropositive one month after this dose.

Protective efficacy of the Pa component:

As the immune response to pertussis antigens following INFANRIX-IPV administration is equivalent to that of Infanrix, it can be assumed that the protective efficacy of the two vaccines will also be equivalent.

The clinical protection of the DTPa component, against WHO-defined typical pertussis (≥ 21 days of paroxysmal cough) 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%.

- a NIH (National Institute of Health - USA) sponsored efficacy study performed in Italy (2,4,6 months schedule). The vaccine efficacy was found to be 84%. In a follow-up study of the same cohort, the efficacy was confirmed for up to 4 years of age.

Immune response to the IPV component:

One month after the primary vaccination, the overall seropositivity for each of the three serotypes (type 1, 2 and 3) was ≥ 99.5%.

Following administration of a booster dose of INFANRIX-IPV, 100% of children were seropositive for the three serotypes.

In all booster trials, vaccination induced a marked increase in antibody levels with respect to pre-booster values.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety, specific toxicity and compatibility of ingredients.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Sodium chloride,
- Aluminium salts,
- Medium 199 (as stabilizer including amino acids mineral salts and vitamins),
- Water for injections.

Residues:

- Neomycin sulfate
- Polymyxin B sulfate

6.2 Incompatibilities

INFANRIX-IPV should not be mixed with other vaccines in the same syringe.

6.3 Shelf life

3 years.

The expiry date of the vaccine is indicated on the label and packaging.

6.4 Special precautions for storage

INFANRIX-IPV should be stored at +2°C to +8°C.

The vaccine should not be frozen. Discard if it has been frozen.

6.5 Nature and contents of container

0.5 mL of suspension in a pre-filled syringe (type I glass) with a plunger stopper (butyl rubber) and with a rubber tip cap.

The tip cap and rubber plunger stopper of the pre-filled syringe are not made with natural rubber latex.

INFANRIX-IPV is supplied in pack sizes of 1 and 10.

Not all pack sizes may be distributed in New Zealand.

6.6 Special precautions for disposal and other handling

The vaccine should be 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. Since a white sediment may form during storage, INFANRIX-IPV should be well shaken.

Any unused product 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: 3 May 2001

10. DATE OF REVISION OF THE TEXT

6 March 2023

Summary table of changes:

Section changed	Summary of new information
4.2	Introduction of pictograms for the pre-filled syringe

6.5	Update to description of syringe and cap, including a statement that tip cap and rubber plunger stopper are not made of natural rubber latex

Version 7.0