Infanrix™-IPV

1. NAME OF THE MEDICINAL PRODUCT
Infanrix™-IPV
Combined diphtheria-tetanus-acellular pertussis and inactivated polio.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Suspension for injection.

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[1]	25 micrograms
Filamentous haemagglutinin[1]	25 micrograms
Pertactin[1]	8 micrograms
Poliovirus (inactivated)	
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

Infanrix™-IPV is a turbid white suspension. Upon storage, a white deposit and clear supernatant can be observed. This does not constitute a sign of deterioration.

3. PHARMACEUTICAL FORM
Suspension for injection.

4. CLINICAL PARTICULARS
4.1 Therapeutic Indications
Infanrix™-IPV is indicated for active 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 who have previously been immunised with ***diphtheria, tetanus, pertussis*** **(**DTP) and polio antigens.

4.2 Posology and Method of Administration
Posology
The primary vaccination schedule consists of three doses in the first year of life and can start from the age of 2 months. An interval of at least 1 month should be respected between subsequent doses.

When the primary course is completed before the age of 6 months, a booster dose can be given in the second year of life. An interval of at least 6 months after completion of primary

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

Infanrix™-IPV should be used in accordance with available official recommendations.

Method of administration

Infanrix™-IPV is for deep intramuscular injection. For infants, the preferred site of injection 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 Contra-indications

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 polio vaccines.

Infanrix™-IPV is contra-indicated 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 Special 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 contra-indication.

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) immunization

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) and 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 contra-indication.

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 $\leq$ 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 Medicinal Products and Other Forms of Interaction

It is ***routine*** practice in paediatric vaccination to coadminister 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 Use During Pregnancy and Lactation

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

Clinical trials 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 to < 1/10*
Uncommon : ≥ *1/1000 to < 1/100*
Rare : ≥ *1/10000 to < 1/1000*
Very rare : < *1/10000*

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, thoracic and mediastinal disorders
Apnoea[2] [see section Special Warnings and Special 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.

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.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic Properties
Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code J07CA02

- Immune response to the DT components:

One month after a primary vaccination course more than 99% of infants vaccinated with **Infanrix™-IPV** had antibody titres 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 titres 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 sponsored efficacy study performed in Italy (2, 4, 6 months schedule) the vaccine efficacy was found to be 84%. In a follow-up 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sodium chloride, , Medium 199 (as stabilizer), water for injections. Potassium chloride, disodium phosphate, monopotassium phosphate, polysorbate 80, glycine, formaldehyde, neomycin sulfate, polymyxin B sulphate are present as residuals from the manufacturing process.

6.2 Incompatibilities

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

6.3 Shelf Life

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

6.4 Special Precautions for Storage

Infanrix™-IPV vaccine has to be stored at +2°C to +8°C.
The **Infanrix™-IPV** vaccine should not be frozen. Discard if it has been frozen.

6.5 Nature and Contents of Container

The **Infanrix™-IPV** vaccine is presented in a prefilled syringe. The prefilled syringes are made of neutral glass type I, which conforms to European Pharmacopoeia Requirements.

6.6 Instructions for Use and Handling

Infanrix™-IPV 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** suspension should be well shaken.

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

Not all presentations are available in every country.

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Thailand) Ltd.

8. MARKETING AUTHORISATION NUMBER

2C 14/51 (N)

9. DATE OF FIRST AUTHORISATION

11 April 2008

Infanrix is a trademark of the GSK group of companies.

Version number: [GDS10/IPIv06] / Date of issue: [04/11/2014]

Manufacturer:
GlaxoSmithKline Biologicals
89, rue de l'Institut - 1330 Rixensart
Belgium

Tel: (32) 2 656 81 11 Fax: (32) 2 656 80 00