Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

IPV Infanrix suspension for injection in pre-filled syringe Diphtheria, tetanus, pertussis (acellular, component) and poliomyelitis (inactivated) vaccine (adsorbed)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 ml) contains:

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

[1]adsorbed on aluminium hydroxide,hydrated 0.5 milligrams Al^{3+}
[2]propagated in VERO cells

The vaccine may contain traces of formaldehyde, neomycin and polymyxin which are used during the manufacturing process (see section 4.3).

Excipients with known effect
The vaccine contains para-aminobenzoic acid < 0.07 nanograms per dose and phenylalanine 0.036 micrograms per dose (see section 4.4).
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe.
IPV Infanrix is a turbid white suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This vaccine is indicated for booster vaccination against diphtheria, tetanus, pertussis, and poliomyelitis diseases in individuals from 16 months to 13 years of age inclusive who have previously recieved primary immunisation series against these diseases.

The administration of IPV Infanrix should be based on official recommendations.

4.2 Posology and method of administration

Posology
A single dose of 0.5 ml should be administered.

IPV Infanrix may be administered to subjects who have previously received whole cell or acellular pertussis-containing vaccines, and oral live attenuated or injected inactivated poliomyelitis vaccines. *(See also sections 4.8 and 5.1).*
Method of administration
The vaccine is for intramuscular injection, usually into the deltoid muscle. However, the anterolateral thigh may be used in very young subjects if preferred.

Do not administer intravascularly.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1 or neomycin, polymyxin or formaldehyde.

Hypersensitivity after previous administration of diphtheria, tetanus, pertussis, or polio vaccines.

IPV 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 pertussis vaccination should be discontinued and the vaccination should be continued with diphtheria-tetanus and polio vaccines.

As with other vaccines, administration of IPV Infanrix should be postponed in subjects suffering from an acute severe febrile illness. The presence of a minor infection is not a contra-indication.

4.4 Special warnings and precautions for use

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.

Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events). A family history of convulsions or a family history of Sudden Infant Death Syndrome (SIDS) does not constitute a contra-indication.

If any of the following events are known to have occurred in temporal relation to receipt of pertussis-containing vaccine, the decision to give further doses of pertussis-containing vaccines should be carefully considered:
- temperature of ≥ 40.0°C within 48 hours, not due to another identifiable cause,
- collapse or shock-like state (hypotonic-hyporesponsiveness 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.

There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks.

As for any vaccination, the risk-benefit of immunising with IPV Infanrix or deferring this vaccination should be weighed carefully in an infant or in a child suffering from a new onset or progression of a severe neurological disorder.

IPV 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.

HIV infection is not considered as a contra-indication. The expected immunological response may not be obtained after vaccination of immunosuppressed patients.

For children under immunosuppressive treatment (corticosteroid therapy, antimitotic chemotherapy, etc.), it is recommended to postpone vaccination until the end of treatment.

IPV Infanrix should under no circumstances be administered intravascularly.
Syncope (fainting) can occur following, or even before, any vaccination especially in adolescents as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance, paraesthesia and tonic-clonic limb movements during recovery. It is important that procedures are in place to avoid injury from faints.

Excipients with known effect
IPV Infanrix contains para-aminobenzoic acid. It may cause allergic reactions (possibly delayed), and exceptionally, bronchospasm.
The vaccine contains 0.036 microgram phenylalanine in each dose.Phenylalanine may be harmful if you have phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

The vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.
The vaccine contains potassium, less than 1 mmol (39 mg) per dose, i.e. essentially 'potassium-free'.

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

4.5 Interaction with other medicinal products and other forms of interaction

IPV Infanrix has been administered concomitantly with measles-mumps-rubella vaccine, varicella vaccine or Hib vaccine in clinical trials. The data available do not suggest any clinically relevant interference in the antibody response to each of the individual antigens.

Interaction studies have not been carried out with other vaccines, biological products or therapeutic medications. However, in accordance with commonly accepted immunisation guidelines, since IPV Infanrix is an inactivated product, there is no theoretical reason why it should not be administered concomitantly with other vaccines or immunoglobulins at separate sites.

As with other vaccines it may be expected that in patients receiving immunosuppressive therapy or patients with immunodeficiency, a protective immune response to one or more antigens in the vaccine may not be achieved.

4.6 Fertility, pregnancy and lactation

It is anticipated that IPV Infanrix would only rarely be administered to subjects of child-bearing potential. Adequate human data on theuse of IPV Infanrix during pregnancy and lactation are not availableand animal studies on reproductive toxicity have not been conducted. Consequently the use of this combined vaccine is not recommended during pregnancy. It is preferable to avoid the use of this vaccine during lactation.

4.7 Effects on ability to drive and use machines

It is anticipated that IPV Infanrix would only rarely be administered to subjects who would be driving or using machines. However, somnolence, commonly reported after vaccination, may temporarily affect the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile
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 IPV Infanrix with respect to the primary course.

List of adverse reactions

Frequencies per dose are defined as follows:

Very common: (≥ 1/10)
Common: (≥1/100 to <1/10)
Uncommon: (≥1/1,000 to <1/100)
Rare: (≥1/10,000 to <1/1,000)
Very rare: (<1/10,000)

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Clinical trial data

Blood and lymphatic system disorders
Rare: lymphadenopathy

Nervous system disorders

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

Respiratory, thoracic and mediastinal disorders
Rare: bronchitis[1], cough[1]

Gastrointestinal disorders
Common: diarrhoea, vomiting, nausea

Skin and subcutaneous tissue disorders
Uncommon: dermatitis allergic, rash[1]
Rare: pruritus, urticaria

Metabolism and nutrition disorders
Very common: appetite lost

General disorders and administration site conditions
Very common: fever ≥38.0°C, pain, redness and swelling at the injection site*
Common: fever >39.5°C, malaise, injection site reactions including induration, asthenia

Psychiatric disorders
Very common: crying abnormal, irritability, restlessness

* Information on extensive swelling of the injected limb (defined as swelling with a diameter > 50 mm, noticeable diffuse swelling or noticeable increase of limb circumference) occurring after IPV Infanrix was actively solicited in two clinical trials. When IPV Infanrix was administered as either a fourth dose or a fifth dose of DTPa to children 4-6 years of age, extensive injection site swelling was reported with incidences of 13% and 25% respectively. The most frequent reactions were large, localised swelling (diameter > 50 mm) occurring around the injection site. A smaller percentage of children (3% and 6% respectively) experiences diffuse swelling of the injected limb, sometimes involving adjacent joint. In general, these reactions began within 48 hours of vaccination and spontaneously resolved over an average of 4 days without sequelae.

Post-marketing data

Blood and lymphatic system disorders
Thrombocytopenia[2]

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[1]

Skin and subcutaneous tissue disorders
Angioneurotic oedema[1]

General disorders and administration site conditions
Injection site vesicles

Immune system disorders
Allergic reactions, including anaphylactic[1] and anaphylactoid reactions

[1]reported with GSK's DTPa containing vaccines
[2]reported with D and T vaccines

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected

adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

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

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code: J07CA02

5.1 Pharmacodynamic properties

The immune response after booster vaccination with IPV Infanrix was evaluated in 917 vaccinees. The immune response observed was independent of the number of doses and type of vaccines administered previously (DTPw or DTPa, OPV or IPV) as shown in the tables below.

One month after vaccination of children aged 15 to 26 months, the immune responses were the following:

Antigen	Previous vaccination history/schedule (N subjects)	3 doses of DTPw + IPV 2, 3, 4 months (N = 37)	3 doses of DTPa + IPV 2, 3, 4 / 2, 4, 6 / 3, 4, 5 or 3, 4.5, 6 months (N = 252)
Diphtheria	% vaccinees with titres ≥0.1 IU/ml by ELISA*	100	99.6
Tetanus	% vaccinees with titres ≥0.1 IU/ml by ELISA*	100	100
Pertussis Pertussis toxoid Filamentous haemagglutinin Pertactin	% vaccinees with titres ≥5 EL.U/ml by ELISA	 100 100 100	 100 100 100
Polio type 1 type 2 type 3	% vaccinees with titres ≥8 by neutralisation*	 100 100 100	 100 100 100

* These levels are considered to be protective

One month after vaccination of children aged 4-7 years, the immune responses were the following:

Antigen	Previous vaccination history/schedule (N subjects)	3 doses of DTPw + IPV 3, 5, 11 months (N = 128)	3 doses of DTPa + IPV or OPV 3, 5, 11-12 months (N = 208)	4 doses of DTPw + IPV 2, 3, 4 + 16-18 months (N = 73)	4 doses of DTPa + IPV or OPV 2, 4, 6 + 18 months (N = 166)
Diphtheria	% vaccinees with titres ≥ 0.1 IU/ml by ELISA*	100	99.0	100	100
Tetanus	% vaccinees with titres ≥ 0.1 IU/ml by ELISA*	100	100	100	100
Pertussis Pertussis toxoid Filamentous haemagglutinin Pertactin	% vaccinees with titres ≥ 5 EL.U/ml by ELISA	 98.3 100 100	 100 100 100	 95.5 100 100	 99.4 100 100
Polio type 1 type 2 type 3	% vaccinees with titres ≥ 8 by neutralisation*	 100 100 100	 100 100 99.5	 100 100 100	 100 100 100

* These levels are considered to be protective

One month after vaccination of children/adolescents aged 10-13 years, the immune responses were the following:

Antigen	Previous vaccination history/schedule (N subjects)	4 doses of DTPw+IPV at 2, 3, 4 + 16-18 months + 1 dose of DT-IPV at 5-6 years (N = 53)
Diphtheria	% vaccinees with titres ≥ 0.1 IU/ml by ELISA*	100
Tetanus	% vaccinees with titres ≥ 0.1 IU/ml by ELISA*	100
Pertussis Pertussis toxoid Filamentous haemagglutinin Pertactin	% vaccinees with titres ≥ 5 EL.U/ml by ELISA	 100 100 100
Polio type 1 type 2 type 3	% vaccinees with titres ≥ 8 by neutralisation*	 100 100 100

* These levels are considered to be protective

After vaccination, ≥ 99% of all subjects had protective antibody levels against diphtheria, tetanus and the three poliovirus types.

No serological correlate of protection has been defined for the pertussis antigens. The antibody titres to the three pertussis components were in all cases higher than those observed after primary vaccination with the paediatric acellular pertussis combination vaccine (DTPa, *Infanrix*™), for which efficacy has been demonstrated in a household contact efficacy study. Based on these comparisons, it can therefore be anticipated that IPV Infanrix would provide protection against pertussis, although the degree and duration of protection afforded by the vaccine are undetermined.

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
Medium 199 (as stabilizer containing amino acids (including phenylalanine), mineral salts (including sodium and potassium), vitamins (including para-aminobenzoic acid) and other substances)
Water for injections

For adjuvants, see section 2.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).

Do not freeze.

Store in the original package, in order to protect from light.

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.

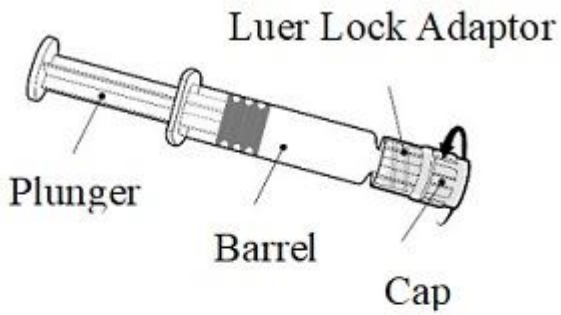
The tip cap and rubber plunger stopper of the pre-filled syringe are made with synthetic rubber.

Pack sizes of 1 and 10, with or without needles.

6.6 Special precautions for disposal and other handling

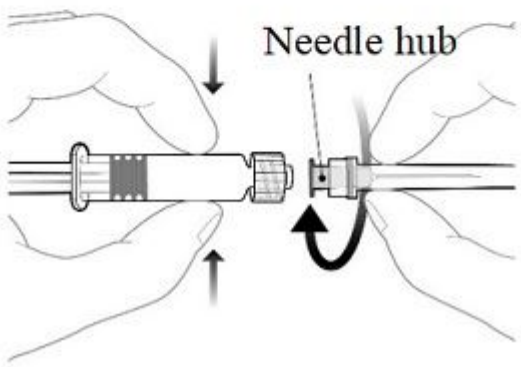
Upon storage, a white deposit and clear supernatant may be observed. This does not constitute a sign of deterioration.
The syringe should be well shaken in order to obtain a homogeneous turbid white suspension.
The suspension should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.

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.

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

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1077/108/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 5th August 2005
Date of last renewal: 7th August 2006

10 DATE OF REVISION OF THE TEXT

May 2023