

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Infanrix-IPV+Hib – powder and suspension for suspension for injection

Diphtheria, tetanus, pertussis (acellular component), poliomyelitis (inactivated) and *Haemophilus influenzae* type b conjugate vaccine (adsorbed)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

A 0.5 ml dose of vaccine 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 µg
Filamentous haemagglutinin ¹	25 µg
Pertactin ¹	8 µg

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

Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate)

10 µg

conjugated to tetanus toxoid as carrier protein approximately 30 µg

¹Adsorbed on aluminium hydroxide, hydrated 0.5 milligrams Al³⁺

²Propagated in VERO cells

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder and suspension for suspension for injection.

The diphtheria, tetanus, acellular pertussis and inactivated poliomyelitis (DTPa-IPV) component is a turbid white suspension.

The lyophilised *Haemophilus influenzae* type b (Hib) component is a white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

INFANRIX-IPV+Hib is indicated for active immunisation against diphtheria, tetanus, pertussis, poliomyelitis and *Haemophilus influenzae* type b disease from the age of 2 months.

4.2 Posology and method of administration

Posology

Primary vaccination:

The primary vaccination schedule consists of two or three doses given in accordance with official recommendations. The minimum age at the time of the first dose is 2 months. Subsequent doses of the primary course should be separated by a minimum interval of four weeks.

Booster vaccination:

After primary vaccination with two doses, a booster dose of INFANRIX-IPV+Hib must be given at least 6 months after the last priming dose, preferably between 11 and 13 months of age.

After primary vaccination with three doses, a booster dose of Hib conjugate vaccine (monovalent or combined) must be administered. The timing of this Hib conjugate vaccine booster dose should be in accordance with official recommendations. INFANRIX-IPV+Hib may be used for this booster dose if administration of the additional antigens at the same time is in accordance with official recommendations.

INFANRIX-IPV+Hib may be used as a booster dose for children who have previously been immunised with other vaccines that contain DTP, polio and Hib antigens.

Paediatric population:

The safety and efficacy of INFANRIX-IPV+Hib in children over 36 months of age have not been established. No data are available.

Method of administration

INFANRIX-IPV+Hib is for deep intramuscular injection, in the anterolateral aspect of the thigh.

It is preferable that each subsequent dose is given into alternating limbs.

INFANRIX-IPV+Hib 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.

INFANRIX-IPV+Hib should under no circumstances be administered intravascularly.

For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients or neomycin, polymyxin and polysorbate 80.

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

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

As with other vaccines, the administration of INFANRIX-IPV+Hib should be postponed in subjects suffering from an acute severe febrile illness. The presence of a minor infection, however, 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.

If any of the following events have occurred in temporal relation to receipt of any DTP-containing vaccine, the decision to give subsequent doses of vaccine containing a pertussis component should be carefully considered.

- Temperature of ≥ 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 ≥ 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, particularly since the events are not associated with permanent sequelae. According to available clinical data, the risk of such reactions is lower with acellular pertussis vaccines than with whole cell pertussis vaccines.

As for any vaccination, the risk-benefit of immunising with INFANRIX-IPV+Hib 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.

The Hib component of the vaccine does not protect against diseases due to other types of *Haemophilus influenzae* nor against meningitis caused by other organisms.

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, IPV and/or Hib vaccination do not constitute contra-indications to administration of INFANRIX-IPV+Hib.

Human Immunodeficiency Virus (HIV) infection is not considered to be a contra-indication to administration of INFANRIX-IPV+Hib.

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

Excretion of capsular polysaccharide antigen in the urine has been described following receipt of Hib vaccines. Therefore false positive antigen detection test results are possible within 1-2 weeks of vaccination.

Administration of INFANRIX-IPV+Hib should be recorded in the patient's International Vaccination Certificate.

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 the 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

If INFANRIX-IPV+Hib is to be given at the same time as another injectable vaccine(s), the vaccines should always be administered at different injection sites.

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

As INFANRIX-IPV+Hib is not intended for use in adults, information on the safety of the vaccine when used during pregnancy or lactation is not available.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

- *Clinical trials*

The safety profile presented below is based on data from more than 3500 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+Hib with respect to the primary course.

Frequencies per dose are defined as follows:

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: ($< 1/10,000$)

Infections and infestations

Uncommon: upper respiratory tract infection

Blood and lymphatic system disorders

Uncommon: lymphadenopathy

Metabolism and nutrition disorders

Very common: appetite lost

Psychiatric disorders:

Very common: crying abnormal, irritability, restlessness

Nervous system disorders

Very common: somnolence

Respiratory, thoracic and mediastinal disorders

Uncommon: bronchitis, cough, rhinorrhoea

Gastrointestinal disorders

Common: diarrhoea, vomiting

Skin and subcutaneous tissue disorders

Uncommon: urticaria, rash

Rare: pruritus, dermatitis

General disorders and administration site conditions

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

Common: injection site reactions including induration, local swelling at the injection site (> 50 mm)¹

Uncommon: diffuse swelling of the injected limb, sometimes involving the adjacent joint¹, fever² $> 39.5^{\circ}\text{C}$, fatigue

- *Post-marketing surveillance*

Immune system disorders

Allergic reactions (including anaphylactic³ and anaphylactoid reactions)

Nervous system disorders:

Collapse or shock-like state (hypotonic-hyporesponsiveness episode), convulsions (with or without fever)

Respiratory, thoracic and mediastinal disorders:

Apnoea³ [see 4.4 for apnoea in very premature infants (≤ 28 weeks of gestation)]

Skin and subcutaneous tissue disorders:

Angioneurotic oedema³

General disorders and administration site conditions:

Swelling of the entire injected limb¹, injection site vesicles³

¹Children primed with acellular pertussis vaccines are more likely to experience swelling reactions after booster administration in comparison with children primed with whole cell vaccines. These reactions resolve over an average of 4 days.

²common with booster vaccination

³reported with GSK's DTPa containing 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

Not applicable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Bacterial and viral vaccines combined, ATC code J07CA06

Results obtained in the clinical studies for each of the components are summarised in the tables below:

Percentage of subjects with antibody titres \geq assay cut-off after primary vaccination with INFANRIX-IPV+Hib:

Antibody (cut-off)	3-5 months N= 86 (1 trial) %	1.5-3.5-6 months N= 62 (1 trial) %	2-3-4 months N= 337 (3 trials) %	2-4-6 months N= 624 (6 trials) %	3-4-5 months N= 127 (2 trials) %	3-4.5-6 months N=198 (1 trial) %
Anti-diphtheria (0.1 IU/ml)*	94.1	100	98.8	99.3	94.4	99.5
Anti-tetanus (0.1 IU/ml)*	100.0**	100	99.7	99.8	99.2	100
Anti-PT (5 EL.U/ml)	99.5**	100	99.4	100	98.4	100
Anti-FHA (5 EL.U/ml)	99.7**	100	100	100	100	100
Anti-PRN (5 EL.U/ml)	99.0**	100	100	100	100	100
Anti-Polio type 1 (1/8 dilution)*	93.0	ND	99.1	99.5	100	100
Anti-Polio type 2 (1/8 dilution)*	95.3	ND	95.7	99.0	99.2	100
Anti-Polio type 3 (1/8 dilution)*	98.8	ND	100	100	99.2	99.4
Anti-PRP (Hib) (0.15 μg/ml)*	83.7	100	98.5	98.5	100	98.4
Anti-PRP (Hib) (1.0μg/ml)	51.2	87.1	68.5	76.0	97.6	81.2

* cut-off accepted as indicative of protection

** Post dose 2 results from studies where DTPa-HBV-IPV+Hib was administered in a schedule 3, 5 and 11 months of age.

N = numbers of subjects

ND = not determined

Percentage of subjects with antibody titres \geq assay cut-off after booster vaccination with INFANRIX-IPV+Hib:

Antibody (cut-off)	Booster vaccination at 11/12 months of age following a 3-5 month primary course N =184 (1 trial) %	Booster vaccination during the second year of life following a three dose primary course N = 1326 (9 trials) %
Anti-diphtheria (0.1 IU/ml)*	100	99.8
Anti-tetanus (0.1 IU/ml)*	99.9**	99.9

Anti-PT (5 EL.U/ml)	99.9**	99.7
Anti-FHA (5 EL.U/ml)	99.9**	100
Anti-PRN (5 EL.U/ml)	99.5**	99.9
Anti-Polio type 1 (1/8 dilution)*	99.4	99.9
Anti-Polio type 2 (1/8 dilution)*	100	100
Anti-Polio type 3 (1/8 dilution)*	99.4	100
Anti-PRP (Hib) (0.15 µg/ml)*	100	100
Anti-PRP (Hib) (1.0 µg/ml)	96.7	99.2

* cut-off accepted as indicative of protection

** Post dose 3 results from studies where DTPa-HBV-IPV+Hib was administered in a schedule 3, 5 and 11 months of age.

N = numbers of subjects

The effectiveness of the Hib component (when combined with DTPa, DTPa-IPV or DTPa-HBV-IPV) was investigated via an extensive post-marketing surveillance study conducted in Germany. Over a 4.5 year follow-up period, the effectiveness of DTPa+Hib or DTPa-IPV+Hib vaccines was 96.7% for a full primary series and 98.5% for a booster dose (irrespective of priming). Over a seven year follow-up period, the effectiveness of the Hib components of two hexavalent vaccines was 89.6% for a full primary series and 100% for a full primary series plus booster dose (irrespective of the Hib vaccine used for priming).

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

Lyophilised HIB component:

Lactose

Liquid DTPa-IPV component:

Sodium chloride

Medium 199 (as stabilizer containing amino acids, mineral salts, vitamins 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

The shelf life of the vaccine components before reconstitution is 3 years.

After reconstitution, the vaccine should be injected immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should normally not be longer than 8 hours at +2°C to +8°C (in a refrigerator).

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.

For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Powder in vial (type I glass) with stopper (butyl rubber)

0.5ml of suspension in pre-filled syringe (type I glass) with a plunger stopper (butyl rubber) with or without needles.

Pack size of 1, 10, 20, 25, 40, 50 and 100.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Upon storage of the DTPa-IPV suspension, a white deposit and clear supernatant can be observed in the syringe. This is not a sign of deterioration.

The pre-filled syringe should be well shaken to obtain a homogeneous suspension. The DTPa-IPV suspension in the pre-filled syringe, the Hib powder in the vial and the reconstituted vaccine should be inspected visually for any foreign particulate matter and/or abnormal physical appearance prior to administration. In the event of either is observed, the vaccine should be discarded.

The vaccine is reconstituted by adding the entire contents of the pre-filled syringe of DTPa-IPV suspension to the vial containing the Hib powder. The mixture should then be injected immediately. The full reconstitution instructions are:

1. Shake the pre-filled syringe containing the DTPa-IPV suspension
2. Attach a needle to the pre-filled syringe of DTPa-IPV and inject the contents of the syringe into the Hib vial.
3. With the needle still inserted, shake the Hib vial vigorously and examine for complete dissolution.
4. Withdraw the entire mixture back into the syringe.
5. Replace the needle with an appropriate size needle for injection and administer the vaccine.
6. If the vaccine is not administered immediately, shake the solution vigorously again before injection.
7. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Ireland) Limited
Stonemasons Way
Rathfarnham
Dublin 16
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 1077/029/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 February 2002

Date of last renewal: 21 April 2013

10 DATE OF REVISION OF THE TEXT

February 2015