ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Infanrix hexa, Powder and suspension for suspension for injection in a pre-filled syringe.
Diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and *Haemophilus influenzae* type b (Hib) conjugate vaccine (adsorbed).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (0.5 ml) contains:

Diphtheria toxoid[1]	not less than 30 International Units (IU)
Tetanus toxoid[1]	not less than 40 International Units (IU)
Bordetella pertussis antigens	
Pertussis toxoid[1]	25 micrograms
Filamentous Haemagglutinin[1]	25 micrograms
Pertactin[1]	8 micrograms
Hepatitis B surface antigen[2,3]	10 micrograms
Poliovirus (inactivated)	
type 1 (Mahoney strain)[4]	40 D-antigen unit
type 2 (MEF-1 strain)[4]	8 D-antigen unit
type 3 (Saukett strain)[4]	32 D-antigen unit
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 micrograms approximately 25 micrograms

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.5 milligrams Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology
[3]adsorbed on aluminium phosphate ($AlPO_4$) 0.32 milligrams Al^{3+}
[4]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).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and suspension for suspension for injection in a pre-filled syringe.
The diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis (DTPa-HBV-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 hexa is indicated for primary and booster vaccination of infants against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and disease caused by *Haemophilus influenzae* type b.

4.2 Posology and method of administration

Posology

The immunisation schedules for Infanrix hexa should be based on official recommendations.

Primary vaccination:

The primary vaccination schedule consists of three doses of 0.5 ml (such as 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) or two doses (such as 3, 5 months). There should be an interval of at least 1 month between doses.
The Expanded Program on Immunisation schedule (at 6, 10, 14 weeks of age) may only be used if a dose of hepatitis B vaccine has been given at birth.

Locally established immunoprophylactic measures against hepatitis B should be maintained.

Where a dose of hepatitis B vaccine is given at birth, Infanrix hexa can be used as a replacement for supplementary doses of hepatitis B vaccine from the age of six weeks. If a second dose of hepatitis B vaccine is required before this age, monovalent hepatitis B vaccine should be used.

Booster vaccination:

After a vaccination with 2 doses (e.g. 3, 5 months) of Infanrix hexa a booster dose must be given at least 6 months after the last priming dose, preferably between 11 and 13 months of age.

After vaccination with 3 doses (e.g. 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) of Infanrix hexa a booster dose must be given at least 6 months after the last priming dose and preferably before 18 months of age.

Booster doses should be given in accordance with the official recommendations, but, as a minimum, a dose of Hib conjugate vaccine must be administered.
Infanrix hexa can be considered for the booster if the composition is in accordance with the official recommendations.

Paediatric population

The safety and efficacy of Infanrix hexa in children over 36 months of age have not been established.
No data are available.

Method of administration

Infanrix hexa is for deep intramuscular injection, preferably at alternating sites for subsequent injections.

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 listed in section 6.1, or formaldehyde, neomycin and polymyxin.

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

Infanrix hexa is contraindicated if the infant 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 course should be continued with diphtheria-tetanus, hepatitis B, polio and Hib vaccines.

As with other vaccines, administration of Infanrix hexa should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection is not a contraindication.

4.4 Special warnings and precautions for use

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 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 Infanrix hexa 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.

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 hexa 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 hexa should under no circumstances be administered intravascularly or intradermally.

Infanrix hexa will not prevent disease caused by pathogens other than *Corynebacterium diphtheriae*, *Clostridium tetani*, *Bordetella pertussis*, hepatitis B virus, poliovirus or *Haemophilus influenzae* type b. However, it can be expected that hepatitis D will be prevented by immunisation as hepatitis D (caused by the delta agent) does not occur in the absence of hepatitis B infection.

As with any vaccine, a protective immune response may not be elicited in all vaccinees (see section 5.1).

A history of febrile convulsions, a family history of convulsions or Sudden Infant Death Syndrome (SIDS) do not constitute a contraindication for the use of Infanrix hexa. Vaccinees with a history of febrile convulsions should be closely followed up as such adverse events may occur within 2 to 3 days post vaccination.

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

Since the Hib capsular polysaccharide antigen is excreted in the urine, a positive urine test can be observed within 1-2 weeks following vaccination. Other tests should be performed in order to confirm Hib infection during this period.

When Infanrix hexa is co-administered with Prevenar (pneumococcal saccharide conjugated vaccine, adsorbed), the physician should be aware that data from clinical studies indicate that the rate of febrile reactions was higher compared to that occurring following the administration of Infanrix hexa alone. These reactions were mostly moderate (less than or equal to 39°C) and transient (see section 4.8).

Antipyretic treatment should be initiated according to local treatment guidelines.

Limited data in 169 premature infants indicate that Infanrix hexa can be given to premature children. However, a lower immune response may be observed and the level of clinical protection remains unknown.

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.

4.5 Interaction with other medicinal products and other forms of interaction

There are insufficient data with regard to the efficacy and safety of simultaneous administration of Infanrix hexa and Measles-Mumps-Rubella vaccine to allow any recommendation to be made.

Data on concomitant administration of Infanrix hexa with Prevenar (pneumococcal saccharide conjugated vaccine, adsorbed) have shown no clinically relevant interference in the antibody response to each of the individual antigens when given as a 3 dose primary vaccination.

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

4.6 Fertility, pregnancy and lactation

As Infanrix hexa 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 relevant.

4.8 Undesirable effects

Summary of the safety profile

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

Tabulated summary of adverse reactions

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

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)

The following drug-related adverse reactions were reported in clinical studies (data from more than 16,000 subjects) and during post-marketing surveillance.

System Organ Class	Frequency	Adverse events
Blood and lymphatic system disorders	Rare	Lymphadenopathy[2]
Immune system disorders	Rare	Anaphylactic reactions[2], anaphylactoid reactions (including urticaria)[2] Allergic reactions (including pruritus)[2]
Metabolism and nutrition disorders	Very common	Appetite lost
Psychiatric disorders	Very common	Crying abnormal, irritability, restlessness
	Common	Nervousness
Nervous system disorders	Uncommon	Somnolence
	Rare	Collapse or shock-like state (hypotonic-hyporesponsiveness episode)[2]
	Very rare	Convulsions (with or without fever)
Respiratory, thoracic and mediastinal disorders	Uncommon	Cough
	Rare	Apnoea[2] [see section 4.4 for apnoea in very premature infants (≤ 28 weeks of gestation)]
Gastrointestinal disorders	Common	Diarrhoea, vomiting
Skin and subcutaneous tissue disorders	Rare	Rash, Angioedema[2]
	Very rare	Dermatitis
General disorders and administration site conditions	Very common	Fever ≥ 38°C, local swelling at the injection site (≤ 50 mm), fatigue, pain, redness
	Common	Fever >39.5°C, 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 joint[1]
	Rare	Swelling of the entire injected limb[1, 2], extensive swelling reactions[2], injection site mass[2], injection site vesicles[2]

[1] 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. These reactions resolve over an average of 4 days.
[2] Adverse reactions from spontaneous reporting.

- Clinical trials on co-administration:

In clinical studies in which some of the vaccinees received Infanrix hexa concomitantly with Prevenar as a booster (4th) dose of both vaccines, fever ≥ 38.0°C was reported following 43.4% of doses in infants receiving Prevenar and Infanrix hexa at the same time as compared to 30.5% of doses in infants receiving the hexavalent vaccine alone. Fever of greater than 39.5°C was observed following 2.6% and 1.5% of doses in infants receiving Infanrix hexa with or without Prevenar, respectively, (see section 4.4). The incidence of fever following co-administration of the two vaccines in the primary series was lower than that observed after the booster dose.

- Experience with hepatitis B vaccine

In extremely rare cases, paralysis, neuropathy, Guillain-Barré syndrome, encephalopathy, encephalitis and meningitis have been reported. The causal relationship to the vaccine has not been established. Thrombocytopenia has been reported with hepatitis B 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 the national reporting system listed in Appendix V.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code: J07CA09

Immunogenicity

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

Percentage of subjects with antibody titres ≥ assay cut-off one month after primary vaccination with Infanrix hexa

Antibody (cut-off)	**Two doses**	**Three doses**			
	3-5 months N= 530	**2-3-4 months N= 196**	**2-4-6 months N= 1693**	**3-4-5 months N= 1055**	**6-10-14 weeks N= 265**
	%	**%**	**%**	**%**	**%**
Anti-diphtheria (0.1 IU/ml) †	98.0	100.0	99.8	99.7	99.2
Anti-tetanus (0.1 IU/ml) †	100.0	100.0	100.0	100.0	99.6
Anti-PT (5 EL.U/ml)	99.5	100.0	100.0	99.8	99.6
Anti-FHA (5 EL.U/ml)	99.7	100.0	100.0	100.0	100.0
Anti-PRN (5 EL.U/ml)	99.0	100.0	100.0	99.7	98.9
Anti-HBs (10 mIU/ml) †	96.8	99.5	98.9	98.0	98.5*
Anti-Polio type 1 (1/8 dilution) †	99.4	100.0	99.9	99.7	99.6
Anti-Polio type 2 (1/8 dilution) †	96.3	97.8	99.3	98.9	95.7
Anti-Polio type 3 (1/8 dilution) †	98.8	100.0	99.7	99.7	99.6
Anti-PRP (0.15 µg/ml) †	91.7	96.4	96.6	96.8	97.4

N = number of subjects

* in a subgroup of infants not administered hepatitis B vaccine at birth, 77.7% of subjects had anti-HBs titres ≥ 10 mIU/ml

† cut-off accepted as indicative of protection

Percentage of subjects with antibody titres ≥ assay cut-off one month after booster vaccination with Infanrix hexa

Antibody (cut-off)	**Booster vaccination at 11 months of age following a 3-5 month primary course N=532**	**Booster vaccination during the second year of life following a three dose primary course N= 2009**
	%	**%**
Anti-diphtheria (0.1 IU/ml) †	100.0	99.9
Anti-tetanus (0.1 IU/ml) †	100.0	99.9
Anti-PT (5 EL.U/ml)	100.0	99.9
Anti-FHA (5 EL.U/ml)	100.0	99.9
Anti-PRN (5 EL.U/ml)	99.2	99.5
Anti-HBs (10 mIU/ml) †	98.9	98.4
Anti-Polio type 1 (1/8 dilution) †	99.8	99.9
Anti-Polio type 2 (1/8 dilution) †	99.4	99.9
Anti-Polio type 3 (1/8 dilution) †	99.2	99.9
Anti-PRP (0.15 µg/ml) †	99.6	99.7

N = number of subjects
† cut-off accepted as indicative of protection

As the immune response to pertussis antigens following Infanrix hexa administration is equivalent to that of Infanrix, the protective efficacy of the two vaccines is expected to be equivalent.

Efficacy in protecting against pertussis

The clinical protection of the pertussis component of Infanrix, against WHO-defined typical pertussis (≥ 21 days of paroxysmal cough) was demonstrated after 3-dose primary immunisation in the studies tabulated below:

Study	**Country**	**Schedule**	**Vaccine efficacy**	**Considerations**
Household contact study (prospective blinded)	Germany	3,4,5 months	88.7%	Based on data collected from secondary contacts in households where there was an index case with typical pertussis
Efficacy study (NIH sponsored)	Italy	2,4,6 months	84%	In a follow-up of the same cohort, the efficacy was confirmed up to 60 months after completion of primary vaccination without administration of a booster dose of pertussis.

Persistence of the immune response

Protective antibodies against hepatitis B have been shown to persist for at least 3.5 years in more than 90% of children administered four doses of Infanrix hexa. Antibody levels were not different from what was observed in a parallel cohort administered 4 doses of monovalent hepatitis B vaccine.

Post marketing experience

Results of long term follow-up in Sweden demonstrate that acellular pertussis vaccines are efficacious in infants when administered according to the 3 and 5 months primary vaccination schedule, with a booster dose administered at approximately 12 months. However, data indicate that protection against pertussis may be waning at 7-8 years of age with this 3-5-12 month's schedule. This suggests that a second booster dose of pertussis vaccine is warranted in children aged 5-7 years who have previously been vaccinated following this particular schedule.

The effectiveness of the Hib component of Infanrix hexa was investigated via an extensive post-marketing surveillance study conducted in Germany. Over a seven year follow-up period, the effectiveness of the Hib components of two hexavalent vaccines, of which one was Infanrix hexa, 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).

Results of ongoing routine national surveillance in Italy demonstrate that Infanrix hexa is effective in controlling Hib disease in infants when the vaccine is administered according to the 3 and 5 months primary vaccination schedule, with a booster dose administered at approximately 11 months. Over a six year period starting in 2006, where Infanrix hexa was the principal Hib-containing vaccine in use with vaccination coverage exceeding 95%, Hib invasive disease continued to be well controlled, with four confirmed Hib cases reported in Italian children aged less than 5 years through passive surveillance.

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, repeated dose toxicity and compatibility of ingredients.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hib powder:
Lactose anhydrous

DTPa-HBV-IPV suspension:
Sodium chloride (NaCl)
Medium 199 containing principally amino acids, mineral salts, vitamins
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.

After reconstitution: an immediate use is recommended. However the stability has been demonstrated for 8 hours at 21°C after reconstitution.

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.

Stability data indicate that the vaccine components are stable at temperatures up to 25°C for 72 hours. At the end of this period Infanrix hexa should be used or discarded. These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

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

6.5 Nature and contents of container

Powder in a vial (type I glass) with a stopper (butyl).

0.5 ml of suspension in a pre-filled syringe (type I glass) with plunger stoppers (butyl).

Pack sizes of 1, 10, 20 and 50 with or without needles and a multipack of 5 packs, each containing 10 vials and 10 pre-filled syringes, without needles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Upon storage, a clear liquid and white deposit may be observed in the pre-filled syringe containing the DTPa-HBV-IPV suspension. This is a normal observation.

The pre-filled syringe should be well shaken in order to obtain a homogeneous turbid white suspension.

The vaccine is reconstituted by adding the entire contents of the pre-filled syringe to the vial containing the powder. The reconstituted mixture should be well shaken until the powder is completely dissolved prior to administration.

The reconstituted vaccine appears as a slightly more cloudy suspension than the liquid component alone. This is a normal observation.

The vaccine suspension should be inspected visually before and after reconstitution for any foreign particulate matter and/or abnormal physical appearance. If either is observed, discard the vaccine.

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

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89

B-1330 Rixensart, Belgium

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/152/001
EU/1/00/152/002
EU/1/00/152/003
EU/1/00/152/004
EU/1/00/152/005
EU/1/00/152/006
EU/1/00/152/007
EU/1/00/152/008
EU/1/00/152/021

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23 October 2000
Date of latest renewal: 31 August 2010

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

1. NAME OF THE MEDICINAL PRODUCT

Infanrix hexa, Powder and suspension for suspension for injection.
Diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and *Haemophilus influenzae* type b (Hib) conjugate vaccine (adsorbed).

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After reconstitution, 1 dose (0.5 ml) contains:

Diphtheria toxoid[1]	not less than 30 International Units (IU)
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Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 micrograms approximately 25 micrograms

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.5 milligrams Al^{3+}
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The vaccine may contain traces of formaldehyde, neomycin and polymyxin which are used during the manufacturing process (see section 4.3).

For the full list of excipients, see section 6.1.

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4.1 Therapeutic indications

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Primary vaccination:

The primary vaccination schedule consists of three doses of 0.5 ml (such as 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) or two doses (such as 3, 5 months). There should be an interval of at least 1 month between doses.
The Expanded Program on Immunisation schedule (at 6, 10, 14 weeks of age) may only be used if a dose of hepatitis B vaccine has been given at birth.

Locally established immunoprophylactic measures against hepatitis B should be maintained.

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Booster vaccination:

After a vaccination with 2 doses (e.g. 3, 5 months) of Infanrix hexa a booster dose must be given at least 6 months after the last priming dose, preferably between 11 and 13 months of age.

After vaccination with 3 doses (e.g. 2, 3, 4 months; 3, 4, 5 months; 2, 4, 6 months) of Infanrix hexa a booster dose must be given at least 6 months after the last priming dose and preferably before 18 months of age.

Booster doses should be given in accordance with the official recommendations, but, as a minimum, a dose of Hib conjugate vaccine must be administered.
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As with any vaccine, a protective immune response may not be elicited in all vaccinees (see section 5.1).

A history of febrile convulsions, a family history of convulsions or Sudden Infant Death Syndrome (SIDS) do not constitute a contraindication for the use of Infanrix hexa. Vaccinees with a history of febrile convulsions should be closely followed up as such adverse events may occur within 2 to 3 days post vaccination.

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4.8 Undesirable effects

Summary of the safety profile

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

Tabulated summary of adverse reactions

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

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)

The following drug-related adverse reactions were reported in clinical studies (data from more than 16,000 subjects) and during post-marketing surveillance.

System Organ Class	Frequency	Adverse events
Blood and lymphatic system disorders	Rare	Lymphadenopathy[2]
Immune system disorders	Rare	Anaphylactic reactions[2], anaphylactoid reactions (including urticaria)[2] Allergic reactions (including pruritus)[2]
Metabolism and nutrition disorders	Very common	Appetite lost
Psychiatric disorders	Very common	Crying abnormal, irritability, restlessness
	Common	Nervousness
Nervous system disorders	Uncommon	Somnolence
	Rare	Collapse or shock-like state (hypotonic-hyporesponsiveness episode)[2]
	Very rare	Convulsions (with or without fever)
Respiratory, thoracic and mediastinal disorders	Uncommon	Cough
	Rare	Apnoea[2] [see section 4.4 for apnoea in very premature infants (≤ 28 weeks of gestation)]
Gastrointestinal disorders	Common	Diarrhoea, vomiting
Skin and subcutaneous tissue disorders	Rare	Rash, Angioedema[2]
	Very rare	Dermatitis
General disorders and administration site conditions	Very common	Fever ≥ 38°C, local swelling at the injection site (≤ 50 mm), fatigue, pain, redness
	Common	Fever >39.5°C, 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 joint[1]
	Rare	Swelling of the entire injected limb[1, 2], extensive swelling reactions[2], injection site mass[2], injection site vesicles[2]

[1] 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. These reactions resolve over an average of 4 days.
[2] Adverse reactions from spontaneous reporting.

- Clinical trials on co-administration:

In clinical studies in which some of the vaccinees received Infanrix hexa concomitantly with Prevenar as a booster (4th) dose of both vaccines, fever ≥ 38.0°C was reported following 43.4% of doses in infants receiving Prevenar and Infanrix hexa at the same time as compared to 30.5% of doses in infants receiving the hexavalent vaccine alone. Fever of greater than 39.5°C was observed following 2.6% and 1.5% of doses in infants receiving Infanrix hexa with or without Prevenar, respectively, (see section 4.4). The incidence of fever following co-administration of the two vaccines in the primary series was lower than that observed after the booster dose.

- Experience with hepatitis B vaccine

In extremely rare cases, paralysis, neuropathy, Guillain-Barré syndrome, encephalopathy, encephalitis and meningitis have been reported. The causal relationship to the vaccine has not been established. Thrombocytopenia has been reported with hepatitis B 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 the national reporting system listed in Appendix V.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code: J07CA09

Immunogenicity

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

Percentage of subjects with antibody titres ≥ assay cut-off one month after primary vaccination with Infanrix hexa

Antibody (cut-off)	**Two doses**	**Three doses**			
	3-5 months N= 530	**2-3-4 months N= 196**	**2-4-6 months N= 1693**	**3-4-5 months N= 1055**	**6-10-14 weeks N= 265**
	%	**%**	**%**	**%**	**%**
Anti-diphtheria (0.1 IU/ml) †	98.0	100.0	99.8	99.7	99.2
Anti-tetanus (0.1 IU/ml) †	100.0	100.0	100.0	100.0	99.6
Anti-PT (5 EL.U/ml)	99.5	100.0	100.0	99.8	99.6
Anti-FHA (5 EL.U/ml)	99.7	100.0	100.0	100.0	100.0
Anti-PRN (5 EL.U/ml)	99.0	100.0	100.0	99.7	98.9
Anti-HBs (10 mIU/ml) †	96.8	99.5	98.9	98.0	98.5*
Anti-Polio type 1 (1/8 dilution) †	99.4	100.0	99.9	99.7	99.6
Anti-Polio type 2 (1/8 dilution) †	96.3	97.8	99.3	98.9	95.7
Anti-Polio type 3 (1/8 dilution) †	98.8	100.0	99.7	99.7	99.6
Anti-PRP (0.15 µg/ml) †	91.7	96.4	96.6	96.8	97.4

N = number of subjects

* in a subgroup of infants not administered hepatitis B vaccine at birth, 77.7% of subjects had anti-HBs titres ≥ 10 mIU/ml

† cut-off accepted as indicative of protection

Percentage of subjects with antibody titres ≥ assay cut-off one month after booster vaccination with Infanrix hexa

Antibody (cut-off)	**Booster vaccination at 11 months of age following a 3-5 month primary course N=532**	**Booster vaccination during the second year of life following a three dose primary course N= 2009**
	%	**%**
Anti-diphtheria (0.1 IU/ml) †	100.0	99.9
Anti-tetanus (0.1 IU/ml) †	100.0	99.9
Anti-PT (5 EL.U/ml)	100.0	99.9
Anti-FHA (5 EL.U/ml)	100.0	99.9
Anti-PRN (5 EL.U/ml)	99.2	99.5
Anti-HBs (10 mIU/ml) †	98.9	98.4
Anti-Polio type 1 (1/8 dilution) †	99.8	99.9
Anti-Polio type 2 (1/8 dilution) †	99.4	99.9
Anti-Polio type 3 (1/8 dilution) †	99.2	99.9
Anti-PRP (0.15 µg/ml) †	99.6	99.7

N = number of subjects
† cut-off accepted as indicative of protection

As the immune response to pertussis antigens following Infanrix hexa administration is equivalent to that of Infanrix, the protective efficacy of the two vaccines is expected to be equivalent.

Efficacy in protecting against pertussis

The clinical protection of the pertussis component of Infanrix, against WHO-defined typical pertussis (≥ 21 days of paroxysmal cough) was demonstrated after 3-dose primary immunisation in the studies tabulated below:

Study	**Country**	**Schedule**	**Vaccine efficacy**	**Considerations**
Household contact study (prospective blinded)	Germany	3,4,5 months	88.7%	Based on data collected from secondary contacts in households where there was an index case with typical pertussis
Efficacy study (NIH sponsored)	Italy	2,4,6 months	84%	In a follow-up of the same cohort, the efficacy was confirmed up to 60 months after completion of primary vaccination without administration of a booster dose of pertussis.

Persistence of the immune response

Protective antibodies against hepatitis B have been shown to persist for at least 3.5 years in more than 90% of children administered four doses of Infanrix hexa. Antibody levels were not different from what was observed in a parallel cohort administered 4 doses of monovalent hepatitis B vaccine.

Post marketing experience

Results of long term follow-up in Sweden demonstrate that acellular pertussis vaccines are efficacious in infants when administered according to the 3 and 5 months primary vaccination schedule, with a booster dose administered at approximately 12 months. However, data indicate that protection against pertussis may be waning at 7-8 years of age with this 3-5-12 month's schedule. This suggests that a second booster dose of pertussis vaccine is warranted in children aged 5-7 years who have previously been vaccinated following this particular schedule.

The effectiveness of the Hib component of Infanrix hexa was investigated via an extensive post-marketing surveillance study conducted in Germany. Over a seven year follow-up period, the effectiveness of the Hib components of two hexavalent vaccines, of which one was Infanrix hexa, 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).

Results of ongoing routine national surveillance in Italy demonstrate that Infanrix hexa is effective in controlling Hib disease in infants when the vaccine is administered according to the 3 and 5 months primary vaccination schedule, with a booster dose administered at approximately 11 months. Over a six year period starting in 2006, where Infanrix hexa was the principal Hib-containing vaccine in use with vaccination coverage exceeding 95%, Hib invasive disease continued to be well controlled, with four confirmed Hib cases reported in Italian children aged less than 5 years through passive surveillance.

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, repeated dose toxicity and compatibility of ingredients.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hib powder:
Lactose anhydrous

DTPa-HBV-IPV suspension:
Sodium chloride (NaCl)
Medium 199 containing principally amino acids, mineral salts, vitamins
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.

After reconstitution: an immediate use is recommended. However the stability has been demonstrated for 8 hours at 21°C after reconstitution.

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.

Stability data indicate that the vaccine components are stable at temperatures up to 25°C for 72 hours. At the end of this period Infanrix hexa should be used or discarded. These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

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

6.5 Nature and contents of container

Powder in a vial (type I glass) with a stopper (butyl).

0.5 ml of suspension in a vial (type I glass) with a stopper (butyl).

Pack sizes of 1 and 50.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Upon storage, a clear liquid and white deposit may be observed in the vial containing the DTPa-HBV-IPV suspension. This is a normal observation.

The DTPa-HBV-IPV suspension should be well shaken in order to obtain a homogeneous turbid white suspension.

The vaccine is reconstituted by adding the entire contents of the vial containing the DTPa-HBV-IPV suspension by means of a syringe to the vial containing the powder. The reconstituted mixture should be well shaken until the powder is completely dissolved prior to administration.

The reconstituted vaccine appears as a slightly more cloudy suspension than the liquid component alone. This is a normal observation.

The vaccine suspension should be inspected visually before and after reconstitution for any foreign particulate matter and/or abnormal physical appearance. If either is observed, discard the vaccine.

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

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89

B-1330 Rixensart, Belgium

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/152/019
EU/1/00/152/020

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23 October 2000
Date of latest renewal: 31 August 2010

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substances

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89,
1330 Rixensart
Belgium

GlaxoSmithKline Biologicals s.a.
Parc de la Noire Epine 20, rue Flemming,
1300 Wavre
Belgium

Novartis Vaccines and Diagnostics GmbH & Co. KG
Emil-von-Behring-Str. 76,
D-35041 Marburg
Germany

Name and address of the manufacturer responsible for batch release

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89,
1330 Rixensart
Belgium

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic Safety Update Reports**

The marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
1 VIAL AND 1 PRE-FILLED SYRINGE WITHOUT NEEDLE
10 VIALS AND 10 PRE-FILLED SYRINGES WITHOUT NEEDLES
20 VIALS AND 20 PRE-FILLED SYRINGES WITHOUT NEEDLES
50 VIALS AND 50 PRE-FILLED SYRINGES WITHOUT NEEDLES
1 VIAL AND 1 PRE-FILLED SYRINGE WITH 2 NEEDLES
10 VIALS AND 10 PRE-FILLED SYRINGES WITH 20 NEEDLES
20 VIALS AND 20 PRE-FILLED SYRINGES WITH 40 NEEDLES
50 VIALS AND 50 PRE-FILLED SYRINGES WITH 100 NEEDLES

1. NAME OF THE MEDICINAL PRODUCT

Infanrix hexa, Powder and suspension for suspension for injection in a pre-filled syringe
Diphtheria (D), tetanus (T), pertussis (acellular component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and *Haemophilus influenzae* type b (Hib) conjugate vaccine (adsorbed)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml):

Diphtheria toxoid[1]	≥ 30 IU
Tetanus toxoid[1]	≥ 40 IU
Bordetella pertussis antigens (Pertussis toxoid[1], Filamentous haemagglutinin[1], Pertactin[1])	25, 25, 8 micrograms
Hepatitis B surface antigen[2]	10 micrograms
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate)[2] conjugated to tetanus toxoid as carrier protein	10 micrograms approximately 25 micrograms

[1]adsorbed on $Al(OH)_3$	0.5 milligrams Al^{3+}
[2]adsorbed on $AlPO_4$	0.32 milligrams Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
Sodium chloride
Medium 199 containing principally amino acids, mineral salts, vitamins
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and suspension for suspension for injection in a pre-filled syringe
Vial: powder
Pre-filled syringe: suspension

1 vial and 1 pre-filled syringe
1 dose (0.5 ml)

10 vials and 10 pre-filled syringes
10 x 1 dose (0.5 ml)

20 vials and 20 pre-filled syringes
20 x 1 dose (0.5 ml)

50 vials and 50 pre-filled syringes
50 x 1 dose (0.5 ml)

1 vial and 1 pre-filled syringe + 2 needles
1 dose (0.5 ml)

10 vials and 10 pre-filled syringes + 20 needles
10 x 1 dose (0.5 ml)

20 vials and 20 pre-filled syringes + 40 needles
20 x 1 dose (0.5 ml)

50 vials and 50 pre-filled syringes + 100 needles
50 x 1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use
Intramuscular use
Shake well before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP: MM/YYYY

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart, Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/152/001 - 1 vial and 1 pre-filled syringe without needle
EU/1/00/152/002 - 10 vials and 10 pre-filled syringes without needles
EU/1/00/152/003 - 20 vials and 20 pre-filled syringes without needles
EU/1/00/152/004 - 50 vials and 50 pre-filled syringes without needles
EU/1/00/152/005 - 1 vial and 1 pre-filled syringe with 2 needles
EU/1/00/152/006 - 10 vials and 10 pre-filled syringes with 20 needles
EU/1/00/152/007 - 20 vials and 20 pre-filled syringes with 40 needles
EU/1/00/152/008 - 50 vials and 50 pre-filled syringes with 100 needles

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
PACK OF 10 VIALS AND 10 PRE-FILLED SYRINGES WITHOUT NEEDLES FOR MULTIPACK OF 50 (5 X 10) (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Infanrix hexa, Powder and suspension for suspension for injection in a pre-filled syringe
Diphtheria (D), tetanus (T), pertussis (acellular component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and *Haemophilus influenzae* type b (Hib) conjugate vaccine (adsorbed)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml):

Diphtheria toxoid[1]	≥ 30 IU
Tetanus toxoid[1]	≥ 40 IU
Bordetella pertussis antigens (Pertussis toxoid[1], Filamentous haemagglutinin[1], Pertactin[1])	25, 25, 8 micrograms
Hepatitis B surface antigen[2]	10 micrograms
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate)[2] conjugated to tetanus toxoid as carrier protein	10 micrograms approximately 25 micrograms

[1]adsorbed on $Al(OH)_3$	0.5 milligrams Al^{3+}
[2]adsorbed on $AlPO_4$	0.32 milligrams Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
Sodium chloride
Medium 199 containing principally amino acids, mineral salts, vitamins
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and suspension for suspension for injection in a pre-filled syringe
Vial: powder
Pre-filled syringe: suspension

Component of a multipack comprising 5 packs, each containing 10 vials and 10 pre-filled syringes without needles

10 vials and 10 pre-filled syringes
10 x 1 dose (0.5 ml)

Each individual pack cannot be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use
Intramuscular use
Shake before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP: MM/YYYY

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart, Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/152/021 - pack of 50 (5 X 10) without needles

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
MULTIPACK OF 50 (5 X 10) (OUTER WRAPPER LABEL TO BE APPLIED ON TRANSPARENT FOIL, INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Infanrix hexa, Powder and suspension for suspension for injection in a pre-filled syringe
Diphtheria (D), tetanus (T), pertussis (acellular component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and *Haemophilus influenzae* type b (Hib) conjugate vaccine (adsorbed)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml):

Diphtheria toxoid[1]	≥ 30 IU
Tetanus toxoid[1]	≥ 40 IU
Bordetella pertussis antigens (Pertussis toxoid[1], Filamentous haemagglutinin[1], Pertactin[1])	25, 25, 8 micrograms
Hepatitis B surface antigen[2]	10 micrograms
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate)[2] conjugated to tetanus toxoid as carrier protein	10 micrograms approximately 25 micrograms

[1]adsorbed on $Al(OH)_3$	0.5 milligrams Al^{3+}
[2]adsorbed on $AlPO_4$	0.32 milligrams Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
Sodium chloride
Medium 199 containing principally amino acids, mineral salts, vitamins
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and suspension for suspension for injection in a pre-filled syringe
Vial: powder
Pre-filled syringe: suspension

Multipack comprising 5 packs, each containing 10 vials and 10 pre-filled syringes without needles
50 x 1 dose (0.5 ml)

Each individual pack cannot be sold separately

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use
Intramuscular use

Shake before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP: MM/YYYY

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart, Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/152/021 - pack of 50 (5 X 10) without needles

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
1 VIAL AND 1 VIAL
50 VIALS AND 50 VIALS

1. NAME OF THE MEDICINAL PRODUCT

Infanrix hexa, Powder and suspension for suspension for injection
Diphtheria (D), tetanus (T), pertussis (acellular component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and *Haemophilus influenzae* type b (Hib) conjugate vaccine (adsorbed)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 ml):

Diphtheria toxoid[1]	≥ 30 IU
Tetanus toxoid[1]	≥ 40 IU
Bordetella pertussis antigens (Pertussis toxoid[1], Filamentous haemagglutinin[1], Pertactin[1])	25, 25, 8 micrograms
Hepatitis B surface antigen[2]	10 micrograms
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate)[2] conjugated to tetanus toxoid as carrier protein	10 micrograms approximately 25 micrograms

[1]adsorbed on $Al(OH)_3$ — 0.5 milligrams Al^{3+}
[2]adsorbed on $AlPO_4$ — 0.32 milligrams Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
Sodium chloride
Medium 199 containing principally amino acids, mineral salts, vitamins
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and suspension for suspension for injection
Vial: powder
Vial: suspension

1 vial and 1 vial
1 dose (0.5 ml)

50 vials and 50 vials
50 x 1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use
Intramuscular use
Shake well before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP: MM/YYYY

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator
Do not freeze
Store in the original package in order to protect from light

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart, Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/00/152/019 - 1 vial and 1 vial
EU/1/00/152/020 - 50 vials and 50 vials

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
VIAL WITH HIB POWDER

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Hib for Infanrix hexa
Powder for suspension for injection
I.M.

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

LOT:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS PRE-FILLED SYRINGE WITH DTPA HBV IPV SUSPENSION

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

DTPa HBV IPV for Infanrix hexa
Suspension for suspension for injection
I.M.

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

LOT:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (0.5 ml)

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
VIAL WITH DTPA HBV IPV SUSPENSION

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

DTPa HBV IPV for Infanrix hexa
Suspension for suspension for injection
I.M.

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

LOT:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (0.5 ml)

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Infanrix hexa, Powder and suspension for suspension for injection in a pre-filled syringe
Diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and *Haemophilus influenzae* type b (Hib) conjugate vaccine (adsorbed).

Read all of this leaflet carefully before your child receives this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This vaccine has been prescribed for your child only. Do not pass it on to others.
- If your child gets any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Infanrix hexa is and what it is used for

Infanrix hexa is a vaccine used to protect your child against six diseases:

- **Diphtheria:** a serious bacterial infection that mainly affects the airways and sometimes the skin. The airways become swollen causing serious breathing problems and sometimes suffocation. The bacteria also release a poison. This can cause nerve damage, heart problems, and even death.

- **Tetanus**: tetanus bacteria enter the body through cuts, scratches or wounds in the skin. Wounds that are more likely to get tetanus infection are burns, fractures, deep wounds or wounds that have soil, dust, horse manure or wood splinters in them. The bacteria release a poison. This can cause muscle stiffness, painful muscle spasms, fits and even death. The muscle spasms can be strong enough to cause bone fractures of the spine.

- **Whooping cough (Pertussis)**: a highly infectious illness that affects the airways. It causes severe coughing that may lead to problems with breathing. The coughing often has a "whooping" sound. The cough may last for one to two months or longer. Whooping cough can also cause ear infections, chest infections (bronchitis) which may last a long time, lung infections (pneumonia), fits, brain damage and even death.

- **Hepatitis B:** is caused by the hepatitis B virus. It makes the liver swollen. The virus is found in body fluids such as in the vagina, blood, semen or spit (saliva) of infected people.

- **Polio:** a viral infection. Polio is often only a mild illness. However, sometimes it can be very serious and cause permanent damage or even death. Polio can make the muscles unable to move (paralysis). This includes the muscles needed for breathing and walking. The arms or legs affected by the disease may be painfully twisted (deformed).

- ***Haemophilus influenzae* type b (Hib)**: can cause brain swelling (inflammation). This can lead to serious problems such as mental slowness (retardation), cerebral palsy, deafness, epilepsy or partial

blindness. It can also cause swelling of the throat. This can cause death by suffocation. Less commonly, the bacteria can also infect the blood, heart, lungs, bones, joints, and tissues of the eyes and mouth.

How Infanrix hexa works
- Infanrix hexa helps your child's body make its own protection (antibodies). This will protect your child against these diseases.
- As with all vaccines, Infanrix hexa may not fully protect all children who are vaccinated.
- The vaccine cannot cause the diseases that it protects your child from.

2. What you need to know before your child receives Infanrix hexa

Infanrix hexa should not be given:

- if your child is allergic to:
  - Infanrix hexa or any of the ingredients of this vaccine (listed in section 6).
  - formaldehyde.
  - neomycin or polymyxin (antibiotics).

  Signs of an allergic reaction may include itchy skin, rash, shortness of breath and swelling of the face or tongue.
- if your child has had an allergic reaction to any vaccine against diphtheria, tetanus, whooping cough, hepatitis B, polio or *Haemophilus influenzae* type b.
- if your child has had problems of the nervous system within 7 days after previous vaccination with a vaccine against whooping cough
- if your child has a severe infection with a high temperature (over 38°C).
  A minor infection such as a cold should not be a problem, but talk to your doctor first.

Infanrix hexa should not be given if any of the above apply to your child. If you are not sure, talk to your doctor or pharmacist before your child is given Infanrix hexa.

Warnings and precautions

Talk to your doctor or pharmacist before your child is given Infanrix hexa:

- if after previously having Infanrix hexa or another vaccine against whooping cough, your child had any problems, especially:
  - a high temperature (over 40°C) within 48 hours of vaccination
  - a collapse or "shock-like" state within 48 hours of vaccination
  - persistent crying lasting 3 hours or more within 48 hours of vaccination
  - fits with or without a high temperature within 3 days of vaccination
- if your child has an undiagnosed or progressive disease of the brain or epilepsy which is not controlled. After control of the disease the vaccine can be given.
- if your child has a bleeding problem or bruises easily
- if your child tends to have fits when they have a fever, or if there is a history of this in the family.

If any of the above apply to your child (or you are not sure), talk to your doctor or pharmacist before your child is given Infanrix hexa.

Other medicines and Infanrix hexa
Tell your doctor or pharmacist if your child is taking, has recently taken, might take any other medicines or has recently received any other vaccine.

Infanrix hexa contains neomycin and polymyxin

This vaccine contains neomycin and polymyxin (antibiotics). Tell your doctor if your child has had an allergic reaction to these ingredients.

3. How Infanrix hexa is given

How much is given
- Your child will have a total of two or three injections with at least 1 month between each injection.
- You will be told by the doctor or nurse when your child should come back for their next injections.
- If additional injections (boosters) are necessary, the doctor will tell you.

How the vaccine is given
- Infanrix hexa will be given as an injection into a muscle.
- The vaccine should never be given into a blood vessel or into the skin.

If your child misses a dose
- If your child misses an injection which is due, it is important that you make another appointment.
- **Make sure your child finishes the complete vaccination course. If not, your child may not be fully protected against the diseases.**

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them. The following side effects may happen with this vaccine:

Allergic reactions
If your child has an allergic reaction, see your doctor straight away. The signs may include:
- rashes that may be itchy or blistering
- swelling of the eyes and face
- difficulty in breathing or swallowing
- a sudden drop in blood pressure and loss of consciousness.

These signs usually start very soon after the injection has been given. Talk to a doctor straight away if they happen after leaving the doctor's surgery.

See your doctor straight away if your child has any of the following serious side effects:
- collapse
- times when they lose consciousness or have a lack of awareness
- fits – this may be when they have a fever

These side effects have happened very rarely with Infanrix hexa as with other vaccines against whooping cough. They usually happen within 2 to 3 days after vaccination.

Other side effects include:

Very common (these may occur with more than 1 in 10 doses of the vaccine)
- feeling tired
- loss of appetite
- high temperature of 38°C or higher
- swelling, pain, redness where the injection site was given
- unusual crying
- feeling irritable or restless

Common (these may occur with up to 1 in 10 doses of the vaccine)

- diarrhoea
- being sick (vomiting)
- high temperature of more than 39.5°C
- swelling larger than 5 cm or hard lump where the injection was given
- feeling nervous

Uncommon (these may occur with up to 1 in 100 doses of the vaccine)
- feeling sleepy
- cough
- large swelling at the injected limb

Rare (these may occur in with up to 1 in 1,000 doses of the vaccine)
- rash
- swollen glands in the neck, armpit or groin (lymphadenopathy)
- in babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination
- temporarily stopping breathing (apnoea)
- swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (angioedema)
- swelling of the whole injected limb
- blisters where the injection was given

Very rare (these may happen with up to 1 in 10,000 doses of the vaccine)
- itching (dermatitis)

Reporting of side effects
If your child gets any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Infanrix hexa

- Keep this vaccine out of the sight and reach of children.
- Do not use this vaccine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C – 8°C).
- Store in the original package in order to protect from light.
- Do not freeze. Freezing destroys the vaccine.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines your child no longer uses. These measures will help to protect the environment.

6. Contents of the pack and other information

What Infanrix hexa contains

The active substances are:

Diphtheria toxoid[1]	not less than 30 International Units (IU)
Tetanus toxoid[1]	not less than 40 International Units (IU)
Bordetella pertussis antigens	

Pertussis toxoid[1]	25 micrograms
Filamentous Haemagglutinin[1]	25 micrograms
Pertactin[1]	8 micrograms
Hepatitis B surface antigen[2,3]	10 micrograms
Poliovirus (inactivated)	
type 1 (Mahoney strain)[4]	40 D-antigen unit
type 2 (MEF-1 strain)[4]	8 D-antigen unit
type 3 (Saukett strain)[4]	32 D-antigen unit
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 micrograms approximately 25 micrograms

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.5 milligrams Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology
[3]adsorbed on aluminium phosphate ($AlPO_4$) 0.32 milligrams Al^{3+}
[4]propagated in VERO cells

The other ingredients are:
Hib powder: lactose anhydrous
DTPa-HBV-IPV suspension: sodium chloride (NaCl), medium 199 containing principally amino acids, mineral salts, vitamins and water for injections

What Infanrix hexa looks like and contents of the pack

- The diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis (DTPa-HBV-IPV) component is a white, slightly milky liquid presented in a pre-filled syringe (0.5 ml).
- The Hib component is a white powder presented in a glass vial.
- Both components are mixed together just before your child receives the injection. The mixed appearance is a white, slightly milky liquid.
- Infanrix hexa is available in packs of 1, 10, 20 and 50 with or without needles, and a multipack of 5 packs, each containing 10 vials and 10 pre-filled syringes, without needles.
- Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency (EMA) web site: http://www.ema.europa.eu/.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Upon storage, a clear liquid and white deposit may be observed in the pre-filled syringe containing the DTPa-HBV-IPV suspension. This is a normal observation.

The pre-filled syringe should be well shaken in order to obtain a homogeneous turbid white suspension.

The vaccine is reconstituted by adding the entire contents of the pre-filled syringe to the vial containing the powder. The reconstitute mixture should then be well shaken until the powder is completely dissolved prior to administration.

The reconstituted vaccine appears as a slightly more cloudy suspension than the liquid component alone. This is a normal observation.

The vaccine suspension should be inspected visually before and after reconstitution for any foreign particule matter and/or abnormal physical appearance. If either is observed, discard the vaccine.

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

Package leaflet: Information for the user

Infanrix hexa, Powder and suspension for suspension for injection
Diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and *Haemophilus influenzae* type b (Hib) conjugate vaccine (adsorbed).

Read all of this leaflet carefully before your child receives this vaccine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor orpharmacist.
- This vaccine has been prescribed for your child only. Do not pass it on to others.
- If your child gets any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Infanrix hexa is and what it is used for

Infanrix hexa is a vaccine used to protect your child against six diseases:

- **Diphtheria:** a serious bacterial infection that mainly affects the airways and sometimes the skin. The airways become swollen causing serious breathing problems and sometimes suffocation. The bacteria also release a poison. This can cause nerve damage, heart problems, and even death.

- **Tetanus**: tetanus bacteria enter the body through cuts, scratches or wounds in the skin. Wounds that are more likely to get tetanus infection are burns, fractures, deep wounds or wounds that have soil, dust, horse manure or wood splinters in them. The bacteria release a poison. This can cause muscle stiffness, painful muscle spasms, fits and even death. The muscle spasms can be strong enough to cause bone fractures of the spine.

- **Whooping cough (Pertussis)**: a highly infectious illness that affects the airways. It causes severe coughing that may lead to problems with breathing. The coughing often has a “whooping” sound. The cough may last for one to two months or longer. Whooping cough can also cause ear infections, chest infections (bronchitis) which may last a long time, lung infections (pneumonia), fits, brain damage and even death.

- **Hepatitis B:** is caused by the hepatitis B virus. It makes the liver swollen. The virus is found in body fluids such as in the vagina, blood, semen or spit (saliva) of infected people.

- **Polio:** a viral infection. Polio is often only a mild illness. However, sometimes it can be very serious and cause permanent damage or even death. Polio can make the muscles unable to move (paralysis). This includes the muscles needed for breathing and walking. The arms or legs affected by the disease may be painfully twisted (deformed).

- ***Haemophilus influenzae* type b (Hib)**: can cause brain swelling (inflammation). This can lead to serious problems such as mental slowness (retardation), cerebral palsy, deafness, epilepsy or partial

blindness. It can also cause swelling of the throat. This can cause death by suffocation. Less commonly, the bacteria can also infect the blood, heart, lungs, bones, joints, and tissues of the eyes and mouth.

How Infanrix hexa works
- Infanrix hexa helps your child's body make its own protection (antibodies). This will protect your child against these diseases.
- As with all vaccines, Infanrix hexa may not fully protect all children who are vaccinated.
- The vaccine cannot cause the diseases that it protects your child from.

2. What you need to know before your child receives Infanrix hexa

Infanrix hexa should not be given:

- if your child is allergic to:
  - Infanrix hexa or any of the ingredients of the vaccine (listed in section 6).
  - formaldehyde.
  - neomycin or polymyxin (antibiotics).

  Signs of an allergic reaction may include itchy skin, rash, shortness of breath and swelling of the face or tongue.
- if your child has had an allergic reaction to any vaccine against diphtheria, tetanus, whooping cough, hepatitis B, polio or *Haemophilus influenzae* type b.
- if your child has had problems of the nervous system within 7 days after previous vaccination with a vaccine against whooping cough
- if your child has a severe infection with a high temperature (over 38°C).
  A minor infection such as a cold should not be a problem, but talk to your doctor first.

Infanrix hexa should not be given if any of the above applies to your child. If you are not sure, talk to your doctor or pharmacist before your child is given Infanrix hexa.

Warnings and precautions

Talk to your doctor or pharmacist before your child is given Infanrix hexa if:

- if after previously having Infanrix hexa or another vaccine against whooping cough, your child had any problems, especially:
  - a high temperature (over 40°C) within 48 hours of vaccination
  - a collapse or "shock-like" state within 48 hours of vaccination
  - persistent crying lasting 3 hours or more within 48 hours of vaccination
  - fits with or without a high temperature within 3 days of vaccination
- if your child has an undiagnosed or progressive disease of the brain or epilepsy which is not controlled. After control of the disease the vaccine can be given.
- if your child has a bleeding problem or bruises easily
- if your child tends to have fits when they have a fever, or if there is a history of this in the family.

If any of the above apply to your child (or you are not sure), talk to your doctor or pharmacist before your child is given Infanrix hexa.

Other medicines and Infanrix hexa
Tell your doctor or pharmacist if your child is taking, has recently taken, might take any other medicines or has recently received any other vaccine.

Infanrix hexa contains neomycin and polymyxin

This vaccine contains neomycin and polymyxin (antibiotics). Tell your doctor if your child has had an allergic reaction to these ingredients.

3. How Infanrix hexa is given

How much is given
- Your child will have a total of two or three injections with at least 1 month between each injection.
- You will be told by the doctor or nurse when your child should come back for their next injections.
- If additional injections (boosters) are necessary, the doctor will tell you.

How the vaccine is given
- Infanrix hexa will be given as an injection into a muscle.
- The vaccine should never be given into a blood vessel or into the skin.

If your child misses a dose
- If your child misses an injection which is due, it is important that you make another appointment.
- **Make sure your child finishes the complete vaccination course. If not, your child may not be fully protected against the diseases.**

4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them. The following side effects may happen with this vaccine:

Allergic reactions
If your child has an allergic reaction, see your doctor straight away. The signs may include:
- rashes that may be itchy or blistering
- swelling of the eyes and face
- difficulty in breathing or swallowing
- a sudden drop in blood pressure and loss of consciousness

These signs usually start very soon after the injection has been given. Talk to a doctor straight away if they happen after leaving the doctor's surgery.

See your doctor straight away if your child has any of the following serious side effects:
- collapse
- times when they lose consciousness or have a lack of awareness
- fits – this may be when they have a fever

These side effects have happened very rarely with Infanrix hexa as with other vaccines against whooping cough. They usually happen within 2 to 3 days after vaccination.

Other side effects include:

Very common (these may occur with more than 1 in 10 doses of the vaccine)
- feeling tired
- loss of appetite
- high temperature of 38°C or higher
- swelling, pain, redness where the injection was given
- unusual crying
- feeling irritable or restless

Common (these may occur with up to 1 in 10 doses of the vaccine)

- diarrhoea
- being sick (vomiting)
- high temperature of more than 39.5°C
- swelling larger than 5 cm or hard lump where the injection was given
- feeling nervous

Uncommon (these may occur with up to 1 in 100 doses of the vaccine)
- feeling sleepy
- cough
- large swelling at the injected limb

Rare (these may occur with up to 1 in 1,000 doses of the vaccine)
- rash
- swollen glands in the neck, armpit or groin (lymphadenopathy)
- in babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination.
- temporarily stopping breathing (apnoea)
- swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (angioedema)
- swelling of the whole injected limb,
- blisters where the injection was given

Very rare (these may occur with up to 1 in 10,000 doses of the vaccine)
- itching (dermatitis)

Reporting of side effects

If your child gets any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Infanrix hexa

- Keep this vaccine out of the sight and reach of children.
- Do not use this vaccine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C – 8°C).
- Store in the original package in order to protect from light.
- Do not freeze. Freezing destroys the vaccine.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines your child no longer uses. These measures will help to protect the environment.

6. Contents of the pack and other information

What Infanrix hexa contains

- The active substances are:

Diphtheria toxoid[1]	not less than 30 International Units (IU)
Tetanus toxoid[1]	not less than 40 International Units (IU)

Bordetella pertussis antigens	
Pertussis toxoid[1]	25 micrograms
Filamentous Haemagglutinin[1]	25 micrograms
Pertactin[1]	8 micrograms
Hepatitis B surface antigen[2,3]	10 micrograms
Poliovirus (inactivated)	
type 1 (Mahoney strain) [4]	40 D-antigen unit
type 2 (MEF-1 strain) [4]	8 D-antigen unit
type 3 (Saukett strain) [4]	32 D-antigen unit
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate) [3] conjugated to tetanus toxoid as carrier protein	10 micrograms approximately 25 micrograms

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.5 milligrams Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology
[3]adsorbed on aluminium phosphate ($AlPO_4$) 0.32 milligrams Al^{3+}
[4]propagated in VERO cells

The other ingredients are:
Hib powder: lactose anhydrous
DTPa-HBV-IPV suspension: sodium chloride (NaCl), medium 199 containing principally amino acids, mineral salts, vitamins and water for injections

What Infanrix hexa looks like and contents of the pack
- The diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis (DTPa-HBV-IPV) component is a white, slightly milky liquid presented in a glass vial (0.5 ml).
- The Hib component is a white powder presented in a glass vial.
- Both components are mixed together just before your child receives the injection. The mixed appearance is a white, slightly milky liquid.
- Infanrix hexa is available in packs of 1 and 50.
- Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

GlaxoSmithKline Biologicals s.a.
Rue de l'Institut 89
B-1330 Rixensart
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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency (EMA) web site: http://www.ema.europa.eu/.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Upon storage, a clear liquid and white deposit may be observed in the vial containing the DTPa-HBV-IPV suspension. This is a normal observation.

The DTPa-HBV-IPV suspension should be well shaken in order to obtain a homogeneous turbid white suspension.

The vaccine is reconstituted by adding the contents of the vial containing the DTPa-HBV-IPV suspension by means of a syringe to the vial containing the powder. The reconstituted mixture should be well shaken until the powder is completely dissolved prior to administration.

The reconstituted vaccine appears as a slightly more cloudy suspension than the liquid component alone. This is a normal observation.

The vaccine suspension should be inspected visually before and after reconstitution for any foreign particule matter and/or abnormal physical appearance. If either is observed, discard the vaccine.

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