ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

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 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 IU
Tetanus toxoid[1]	not less than 40 IU
Bordetella pertussis antigens	
Pertussis toxoid[1]	25 micrograms
Filamentous Haemagglutinin[1]	25 micrograms
Pertactin[1]	8 micrograms
Hepatitis B surface antigen[2,3]	10 micrograms
Poliovirus (inactivated)	
type 1 (Mahoney strain)	40 D-antigen unit
type 2 (MEF-1 strain)	8 D-antigen unit
type 3 (Saukett strain)	32 D-antigen unit
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 micrograms 20-40 micrograms

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.95 milligrams Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on aluminium phosphate ($AlPO_4$) 1.45 milligrams Al^{3+}

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and suspension for suspension for injection.
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.

Infanrix hexa is not intended for use in children over 36 months of age.

4.2 Posology and method of administration

Posology

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 for the second dose 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 must include at least the Hib conjugate component.

Infanrix hexa can be considered for the booster if the composition is in accordance with the official recommendations.

Method of administration

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

4.3 Contraindications

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

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

Infanrix hexa is contra-indicated 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 contra-indication.

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 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.

The hepatitis B component of the vaccine will not prevent infection caused by other agents such as hepatitis A, hepatitis C and hepatitis E viruses and other pathogens known to infect the liver.

The Hib component of the vaccine does not protect against diseases due to other capsular serotypes than type b of *Haemophilus influenzae* or against meningitis caused by other organisms.

A history of febrile convulsions requires special attention. A family history of convulsions or a family history of Sudden Infant Death Syndrome (SIDS) does not constitute a contra-indication.

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

Excretion of capsular polysaccharide antigen in the urine has been described following receipt of Hib vaccines, and therefore antigen detection may not have a diagnostic value in suspected Hib disease within 1-2 weeks of vaccination.

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.

4.5 Interaction with other medicinal products and other forms of interaction

There are no data with regard to the efficacy and safety of simultaneous administration of Infanrix hexa and Measles-Mumps-Rubella vaccine.

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 or patients with immunodeficiency, an adequate response may not be achieved.

4.6 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

- Clinical trials:

Clinical trials involved the administration of over 13,500 doses of Infanrix hexa to more than 4,500 healthy infants from 6 weeks of age as primary vaccination. More than 2,300 infants 12 to 24 months of age received a booster dose of Infanrix hexa.
No increase in the incidence or severity of these undesirable events was seen with subsequent doses of the primary vaccination series.

As has been observed for DTPa and DTPa-containing combinations, an increase in reactogenicity was reported after booster vaccination with Infanrix hexa with respect to the primary course; however, the incidence of symptoms graded as severe was low.

- Clinical trials on co-administration:

When Infanrix hexa is co-administered with Prevenar, fever ≥ 38°C per dose was reported in 28.3% to 48.3% of infants in the group receiving Prevenar and Infanrix hexa at the same time as compared to 15.6% to 23.4% in the group receiving the hexavalent vaccine alone. Fever of greater than 39.5°C per dose was observed in 0.6% to 2.8% of infants receiving Prevenar and Infanrix hexa (see section 4.4).

- Tabulated summary of adverse events:

Undesirable effects reported in clinical trials (following primary immunisation or booster dose) or reported during post marketing surveillance are listed here below per system organ class. For those symptoms reported both during clinical trials and during PMS, invariably the highest frequencies were under controlled clinical trial conditions.

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

Frequencies are defined as follows:

Very common:	≥ 10%
Common:	≥ 1% and < 10%
Uncommon:	≥ 0.1% and < 1%
Rare:	≥ 0.01% and < 0.1%
Very rare:	< 0.01%

Infections and infestations
Common: viral infection, moniliasis, otitis media, upper respiratory tract infection, pharyngitis
Uncommon: infection

Psychiatric disorders:
Very common: irritability
Common: abnormal crying, restlessness

Nervous system disorders:
Very common: drowsiness
Uncommon: somnolence

Eye disorders
Common: conjunctivitis

Respiratory, thoracic and mediastinal disorders

Common: bronchitis, coughing, rhinitis
Uncommon: bronchospasm, laryngitis, stridor

Gastrointestinal disorders:
Very common: loss of appetite
Common: diarrhoea, enteritis, gastro-enteritis
Uncommon: abdominal pain, vomiting, constipation

Skin and subcutaneous tissue disorders
Common: rash, dermatitis
Uncommon: eczema

General disorders and administration site conditions:
Very common: pain, redness, local swelling at the injection site (≤ 50 mm), fever ≥ 38°C
Common: injection site reaction, local swelling at the injection site (> 50 mm)*, fever >39°C
Uncommon: diffuse swelling of the injected limb, sometimes involving the adjacent joint*, fatigue

- Post marketing surveillance:

Immune system disorders
Allergic reactions (including rash and pruritus), anaphylactoid reactions (including urticaria)

Nervous system disorders:
Convulsions (with or without fever), collapse or shock-like state (hypotonic-hyporesponsiveness episode)

General disorders and administration site conditions:
Injection site mass, injection site induration, swelling of the entire injected limb*

* 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.

- Experience with hepatitis B vaccine:

Nearly 100 million doses of Engerix B 10 µg, GlaxoSmithKline Biologicals' hepatitis B vaccine, have been distributed for infants < 2 years old. 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 very rarely with hepatitis B vaccines.

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 JO7CA

The tetanus and diphtheria toxoids are obtained by formaldehyde treatment of purified *Corynebacterium diphtheriae* and *Clostridium tetani* toxins. The acellular pertussis vaccine components are obtained by extraction and purification from phase I *Bordetella pertussis* cultures, followed by irreversible detoxification of the pertussis toxin by glutaraldehyde and formaldehyde

treatment, and formaldehyde treatment of filamentous haemagglutinin and pertactin. The surface antigen of the HBV is produced by culture of genetically-engineered yeast cells *(Saccharomyces cerevisiae)* which carry the gene coding for the major surface antigen of the HBV and is highly purified. The diphtheria toxoid, tetanus toxoid, acellular pertussis and hepatitis B components are adsorbed onto aluminium salts.

The three polioviruses are cultivated on a continuous VERO cell line, purified and inactivated with formaldehyde.

The DTPa-HBV-IPV components are formulated in saline and contain phenoxyethanol.

The Hib polysaccharide is prepared from Hib, strain 20,752 and after activation with cyanogen bromide and derivatisation with an adipic hydrazide spacer is coupled to tetanus toxoid via carbodiimide condensation. After purification the conjugate is adsorbed on aluminium salt, and then lyophilised in the presence of lactose as stabiliser.

Infanrix hexa meets the World Health Organisation (WHO) requirements for manufacture of biological substances, of diphtheria, tetanus, pertussis and combined vaccines, of hepatitis B vaccines made by recombinant DNA techniques, of inactivated poliomyelitis vaccines and of Hib conjugate vaccines.

Surveillance studies are ongoing and will provide additional information with regard to the duration of protection.

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

- DTPa component:

Immunological data:

One month after a 3-dose primary vaccination course, 98.5 to 100% of infants vaccinated with Infanrix hexa had antibody titres of ≥ 0.1 IU/ml for both tetanus and diphtheria.

Following administration of a 4th dose of Infanrix hexa in the second year of life, 100 % of infants had antibody titres of ≥ 0.1 IU/ml for both tetanus and diphtheria.

One month after a 3-dose primary vaccination course, the overall response rate for each of the three individual pertussis antigens (pertussis toxoid , filamentous haemagglutinin , pertactin) was between 97.2-99.3%, 95.2-100% and 95.9-99.3%, respectively.

Following administration of a 4th dose of Infanrix hexa in the second year of life, a booster response was seen in at least 97.2 %, 94.1% and 100 % of vaccinated infants against the respective pertussis antigens.

Since the serological correlation for protection against pertussis disease does not exist, the efficacy of the pertussis component presently relies on efficacy trials described just hereafter.

Protective efficacy data:

The clinical protection of the DTPa component, against WHO-defined typical pertussis (≥ 21 days of paroxysmal cough) was demonstrated in:

- a prospective blinded household contact study performed in Germany (3, 4, 5 months schedule). Based on data collected from secondary contacts in households where there was an index case with typical pertussis, the protective efficacy of the vaccine was 88.7%.

- a NIH sponsored efficacy study performed in Italy (2, 4, 6 months schedule. The vaccine efficacy was found to be 84%. In a follow-up of the same cohort, the efficacy was confirmed up to 60

months after completion of primary vaccination without administration of a booster dose of pertussis.

- Hepatitis B component:

After a 3-dose primary vaccination course with Infanrix hexa, 98.5 to 100% of infants developed protective antibody titres of ≥ 10 mIU/ml

At one month after the booster dose, 97 to 100 % of these subjects had protective titres of ≥ 10 mIU/ml.

- Inactivated poliovirus (IPV) component:

One month after a 3-dose primary vaccination, the seroprotection rates for each of the three serotypes (types 1, 2 and 3) were 99.2 to 100%, 94.5 to 99.0% and 98.8 to 100%, respectively.
Following administration of the booster dose, at least 98.5 %, 98.5 % and 100 % of infants were seroprotected for the three serotypes, respectively.

- Hib component:

One month after completion of a 3-dose primary vaccination course, the Geometric Mean Concentration (GMC) of antibodies ranged from 1.52 to 3.53 µg/ml, with between 93.5 and 100% of the subjects reaching antibody titres ≥0.15 µg/ml.

One month after the booster dose given in the second year of life, the GMC ranged from 19.1 to 94.0 µg/ml, with 99.5 to 100% of the subjects reaching antibody titres ≥0.15 µg/ml.

These GMCs are lower with respect to separate administration of the Hib component, but they are not different from those elicited by licenced DTPa/Hib and DTPa-IPV/Hib vaccines.

The humoral immune response (as measured by serum antibody levels) is complemented by the induction of a cellular immune response (or immune memory), which has been shown to be present as early as four months after completion of the primary immunisation schedule with Infanrix hexa. Data from field studies in the United Kingdom have shown that Hib vaccine effectiveness remains high for at least 6 years after primary vaccination, despite low levels of serum antibodies and without administration of a booster dose. Immune memory has thus been proposed as an important mechanism resulting in the long-term protection against invasive Hib disease seen in these studies.

The effectiveness of the GlaxoSmithKline Biologicals' Hib component (when combined with DTPa or DTPa-IPV) has been and continues to be investigated via an extensive post-marketing surveillance study conducted in Germany. Over a 2 year follow-up period, the effectiveness of three primary doses of DTPa/Hib or DTPa-IPV/Hib was 98.8%.

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)
Phenoxyethanol (2.5 mg)
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.

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 prefilled syringe (type I glass) with plunger stoppers (butyl).

Pack sizes of 1, 10, 20 and 50 with or without needles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Upon storage, a white deposit and clear supernatant may be observed. This does not constitute a sign of deterioration.

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

The DTPa-HBV-IPV suspension should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.

The vaccine is reconstituted by adding the contents of the syringe to the vial containing the Hib powder. After the addition of the DTPa-HBV-IPV vaccine to the powder, the mixture should be well shaken until the powder is completely dissolved.

The reconstituted vaccine presents as a slightly more cloudy suspension than the liquid component alone. This is normal and does not impair the performance of the vaccine. In the event of other variation being observed, discard the vaccine.

Any unused product of 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

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/10/2000

10. DATE OF REVISION OF THE TEXT

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 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 IU
Tetanus toxoid[1]	not less than 40 IU
Bordetella pertussis antigens	
Pertussis toxoid[1]	25 micrograms
Filamentous Haemagglutinin[1]	25 micrograms
Pertactin[1]	8 micrograms
Hepatitis B surface antigen[2,3]	10 micrograms
Poliovirus (inactivated)	
type 1 (Mahoney strain)	40 D-antigen unit
type 2 (MEF-1 strain)	8 D-antigen unit
type 3 (Saukett strain)	32 D-antigen unit
Haemophilus type b polysaccharide (polyribosylribitol phosphate) [3] conjugated to tetanus toxoid as carrier protein	10 micrograms 20-40 micrograms

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.95 milligrams Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on aluminium phosphate ($AlPO_4$) 1.45 milligrams Al^{3+}

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and suspension for suspension for injection.
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.

Infanrix hexa is not intended for use in children over 36 months of age.

4.2 Posology and method of administration

Posology

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 for the second dose 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 must include at least the Hib conjugate component.

Infanrix hexa can be considered for the booster if the composition is in accordance with the official recommendations.

Method of administration

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

4.3 Contraindications

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

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

Infanrix hexa is contra-indicated 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 contra-indication.

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 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.

The hepatitis B component of the vaccine will not prevent infection caused by other agents such as hepatitis A, hepatitis C and hepatitis E viruses and other pathogens known to infect the liver.

The Hib component of the vaccine does not protect against diseases due to other capsular serotypes than type b of *Haemophilus influenzae* or against meningitis caused by other organisms.

A history of febrile convulsions requires special attention. A family history of convulsions or a family history of Sudden Infant Death Syndrome (SIDS) does not constitute a contra-indication.

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

Excretion of capsular polysaccharide antigen in the urine has been described following receipt of Hib vaccines, and therefore antigen detection may not have a diagnostic value in suspected Hib disease within 1-2 weeks of vaccination.

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.

4.5 Interaction with other medicinal products and other forms of interaction

There are no data with regard to the efficacy and safety of simultaneous administration of Infanrix hexa and Measles-Mumps-Rubella vaccine.

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 or patients with immunodeficiency, an adequate response may not be achieved.

4.6 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

- Clinical trials:

Clinical trials involved the administration of over 13,500 doses of Infanrix hexa to more than 4,500 healthy infants from 6 weeks of age as primary vaccination. More than 2,300 infants 12 to 24 months of age received a booster dose of Infanrix hexa.
No increase in the incidence or severity of these undesirable events was seen with subsequent doses of the primary vaccination series.

As has been observed for DTPa and DTPa-containing combinations, an increase in reactogenicity was reported after booster vaccination with Infanrix hexa with respect to the primary course; however, the incidence of symptoms graded as severe was low.

- Clinical trials on co-administration:

When Infanrix hexa is co-administered with Prevenar, fever ≥ 38°C per dose was reported in 28.3% to 48.3% of infants in the group receiving Prevenar and Infanrix hexa at the same time as compared to 15.6% to 23.4% in the group receiving the hexavalent vaccine alone. Fever of greater than 39.5°C per dose was observed in 0.6% to 2.8% of infants receiving Prevenar and Infanrix hexa (see section 4.4).

- Tabulated summary of adverse events:

Undesirable effects reported in clinical trials (following primary immunisation or booster dose) or reported during post marketing surveillance are listed here below per system organ class. For those symptoms reported both during clinical trials and during PMS, invariably the highest frequencies were under controlled clinical trial conditions.

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

Frequencies are defined as follows:

Very common: ≥ 10%
Common: ≥ 1% and < 10%
Uncommon: ≥ 0.1% and < 1%
Rare: ≥ 0.01% and < 0.1%
Very rare: < 0.01%

Infections and infestations
Common: viral infection, moniliasis, otitis media, upper respiratory tract infection, pharyngitis
Uncommon: infection

Psychiatric disorders:
Very common: irritability
Common: abnormal crying, restlessness

Nervous system disorders:
Very common: drowsiness
Uncommon: somnolence

Eye disorders
Common: conjunctivitis

Respiratory, thoracic and mediastinal disorders
Common: bronchitis, coughing, rhinitis

Uncommon: bronchospasm, laryngitis, stridor

Gastrointestinal disorders:
Very common: loss of appetite
Common: diarrhoea, enteritis, gastro-enteritis
Uncommon: abdominal pain, vomiting, constipation

Skin and subcutaneous tissue disorders
Common: rash, dermatitis
Uncommon: eczema

General disorders and administration site conditions:
Very common: pain, redness, local swelling at the injection site (≤ 50 mm), fever ≥ 38°C
Common: injection site reaction, local swelling at the injection site (> 50 mm)*, fever >39°C
Uncommon: diffuse swelling of the injected limb, sometimes involving the adjacent joint*, fatigue

- Post marketing surveillance:

Immune system disorders
Allergic reactions (including rash and pruritus), anaphylactoid reactions (including urticaria)

Nervous system disorders:
Convulsions (with or without fever), collapse or shock-like state (hypotonic-hyporesponsiveness episode)

General disorders and administration site conditions:
Injection site mass, injection site induration, swelling of the entire injected limb*

** 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.

- Experience with hepatitis B vaccine:

Nearly 100 million doses of Engerix B 10 µg, GlaxoSmithKline Biologicals' hepatitis B vaccine, have been distributed for infants < 2 years old. 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 very rarely with hepatitis B vaccines.

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 JO7CA

The tetanus and diphtheria toxoids are obtained by formaldehyde treatment of purified *Corynebacterium diphtheriae* and *Clostridium tetani* toxins. The acellular pertussis vaccine components are obtained by extraction and purification from phase I *Bordetella pertussis* cultures, followed by irreversible detoxification of the pertussis toxin by glutaraldehyde and formaldehyde

treatment, and formaldehyde treatment of filamentous haemagglutinin and pertactin. The surface antigen of the HBV is produced by culture of genetically-engineered yeast cells *(Saccharomyces cerevisiae)* which carry the gene coding for the major surface antigen of the HBV and is highly purified. The diphtheria toxoid, tetanus toxoid, acellular pertussis and hepatitis B components are adsorbed onto aluminium salts.

The three polioviruses are cultivated on a continuous VERO cell line, purified and inactivated with formaldehyde.

The DTPa-HBV-IPV components are formulated in saline and contain phenoxyethanol.

The Hib polysaccharide is prepared from Hib, strain 20,752 and after activation with cyanogen bromide and derivatisation with an adipic hydrazide spacer is coupled to tetanus toxoid via carbodiimide condensation. After purification the conjugate is adsorbed on aluminium salt, and then lyophilised in the presence of lactose as stabiliser.

Infanrix hexa meets the World Health Organisation (WHO) requirements for manufacture of biological substances, of diphtheria, tetanus, pertussis and combined vaccines, of hepatitis B vaccines made by recombinant DNA techniques, of inactivated poliomyelitis vaccines and of Hib conjugate vaccines.

Surveillance studies are ongoing and will provide additional information with regard to the duration of protection.

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

- DTPa component:

Immunological data:

One month after a 3-dose primary vaccination course, 98.5 to 100% of infants vaccinated with Infanrix hexa had antibody titres of ≥ 0.1 IU/ml for both tetanus and diphtheria.

Following administration of a 4th dose of Infanrix hexa in the second year of life, 100 % of infants had antibody titres of ≥ 0.1 IU/ml for both tetanus and diphtheria.

One month after a 3-dose primary vaccination course, the overall response rate for each of the three individual pertussis antigens (pertussis toxoid , filamentous haemagglutinin , pertactin) was between 97.2-99.3%, 95.2-100% and 95.9-99.3%, respectively.

Following administration of a 4th dose of Infanrix hexa in the second year of life, a booster response was seen in at least 97.2 %, 94.1% and 100 % of vaccinated infants against the respective pertussis antigens.

Since the serological correlation for protection against pertussis disease does not exist, the efficacy of the pertussis component presently relies on efficacy trials described just hereafter.

Protective efficacy data:

The clinical protection of the DTPa component, against WHO-defined typical pertussis (≥ 21 days of paroxysmal cough) was demonstrated in:

- a prospective blinded household contact study performed in Germany (3, 4, 5 months schedule). Based on data collected from secondary contacts in households where there was an index case with typical pertussis, the protective efficacy of the vaccine was 88.7%.

- a NIH sponsored efficacy study performed in Italy (2, 4, 6 months schedule. The vaccine efficacy was found to be 84%. In a follow-up of the same cohort, the efficacy was confirmed up to 60

months after completion of primary vaccination without administration of a booster dose of pertussis.

- Hepatitis B component:

After a 3-dose primary vaccination course with Infanrix hexa, 98.5 to 100% of infants developed protective antibody titres of ≥ 10 mIU/ml

At one month after the booster dose, 97 to 100 % of these subjects had protective titres of ≥ 10 mIU/ml.

- Inactivated poliovirus (IPV) component:

One month after a 3-dose primary vaccination, the seroprotection rates for each of the three serotypes (types 1, 2 and 3) were 99.2 to 100%, 94.5 to 99.0% and 98.8 to 100%, respectively.
Following administration of the booster dose, at least 98.5 %, 98.5 % and 100 % of infants were seroprotected for the three serotypes, respectively.

- Hib component:

One month after completion of a 3-dose primary vaccination course, the Geometric Mean Concentration (GMC) of antibodies ranged from 1.52 to 3.53 µg/ml, with between 93.5 and 100% of the subjects reaching antibody titres ≥0.15 µg/ml.

One month after the booster dose given in the second year of life, the GMC ranged from 19.1 to 94.0 µg/ml, with 99.5 to 100% of the subjects reaching antibody titres ≥0.15 µg/ml.

These GMCs are lower with respect to separate administration of the Hib component, but they are not different from those elicited by licenced DTPa/Hib and DTPa-IPV/Hib vaccines.

The humoral immune response (as measured by serum antibody levels) is complemented by the induction of a cellular immune response (or immune memory), which has been shown to be present as early as four months after completion of the primary immunisation schedule with Infanrix hexa. Data from field studies in the United Kingdom have shown that Hib vaccine effectiveness remains high for at least 6 years after primary vaccination, despite low levels of serum antibodies and without administration of a booster dose. Immune memory has thus been proposed as an important mechanism resulting in the long-term protection against invasive Hib disease seen in these studies.

The effectiveness of the GlaxoSmithKline Biologicals' Hib component (when combined with DTPa or DTPa-IPV) has been and continuous to be investigated via an extensive post-marketing surveillance study conducted in Germany. Over a 2 year follow-up period, the effectiveness of three primary doses of DTPa/Hib or DTPa-IPV/Hib was 98.8%.

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)
Phenoxyethanol (2.5 mg)
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.

6.5 Nature and contents of container

Powder in a vial (type I glass) with Bioset® with a stopper (butyl).
0.5 ml of suspension in prefilled syringe (type I glass) with plunger stoppers (butyl).

Pack sizes of 1, 10, 20 and 50 with or without needles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

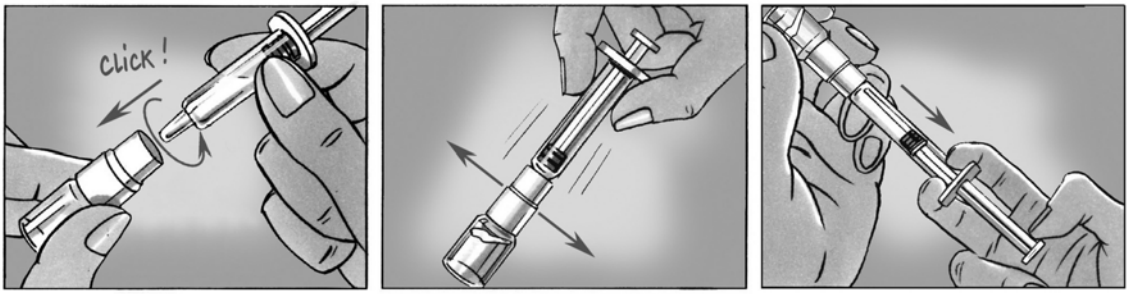
Upon storage, a white deposit and clear supernatant may be observed. This does not constitute a sign of deterioration.

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

The DTPa-HBV-IPV suspension should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, discard the vaccine.

The vaccine is reconstituted by adding the contents of the syringe to the vial containing the Hib powder. It is good clinical practice to only inject a vaccine when it has reached room temperature. In addition, a vial at room temperature ensures sufficient elasticity of the rubber closure to minimise any coring of rubber particles. To achieve this, the vial should be kept at room temperature (25 ± 3 °C) for at least five minutes before connecting the syringe and reconstituting the vaccine. For reconstitution, twist and remove the plastic cover from the Bioset® and remove the cap from the syringe. Before connecting the syringe onto the Bioset®, make sure the two containers are aligned (see Picture 1). Connect the syringe onto the Bioset® by twisting it. Push downwards until syringe“clicks” into

position. Inject the contents of the syringe into the vial. Mix thoroughly until the Hib powder is completely dissolved. Aspirate the reconstituted vaccine back into the syringe. Unscrew the syringe from Bioset® and affix a needle for vaccine administration.



The reconstituted vaccine presents as a slightly more cloudy suspension than the liquid component alone. This is normal and does not impair the performance of the vaccine. In the event of other variation being observed, discard the vaccine.

Any unused 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/1/00/152/009
EU/1/00/152/010
EU/1/00/152/011
EU/1/00/152/012
EU/1/00/152/013
EU/1/00/152/014
EU/1/00/152/015
EU/1/00/152/016
EU/1/00/152/017
EU/1/00/152/018

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/10/2000

10. DATE OF REVISION OF THE TEXT

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURING AUTHORISATION HOLDER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OF THE MARKETING AUTHORISATION

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCES AND MANUFACTURING AUTHORISATION HOLDER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substances

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

Chiron-Behring
Postfach 1140
3550 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 OF THE MARKETING AUTHORISATION

- **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER**

Medicinal product subject to medical prescription.

- **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

Not applicable.

- **OTHER CONDITIONS**

The holder of the marketing authorisation must inform the European Commission about the marketing plans for the medicinal product authorised by this decision.

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

The holder of marketing authorisation will continue to submit annual PSURs.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
PACK SIZE OF 1 VIAL AND 1 PREFILLED SYRINGE WITHOUT NEEDLE

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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
Syringe: suspension
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/001

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
PACK SIZE OF 10 VIALS AND 10 PREFILLED SYRINGES WITHOUT NEEDLE

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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
Syringe: suspension
10 x 1 dose
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/002

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING PACK SIZE OF 20 VIALS AND 20 PREFILLED SYRINGES WITHOUT NEEDLE

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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
Syringe: suspension
20 x 1 dose
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/003

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
PACK SIZE OF 50 VIALS AND 50 PREFILLED SYRINGES WITHOUT NEEDLE

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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
Syringe: suspension
50 x 1 dose
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/004

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING PACK SIZE OF 1 VIAL AND 1 PREFILLED SYRINGE WITH NEEDLE

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate) [3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
$Al(OH)_3$
$AlPO_4$
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
Syringe: suspension
Needles
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/005

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING PACK SIZE OF 10 VIALS AND 10 PREFILLED SYRINGES WITH NEEDLE

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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
Syringe: suspension
Needles
10 x 1 dose
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/006

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
PACK SIZE OF 20 VIALS AND 20 PREFILLED SYRINGES WITH NEEDLE

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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
Syringe: suspension
Needles
20 x 1 dose
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/007

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
PACK SIZE OF 50 VIALS AND 50 PREFILLED SYRINGES WITH NEEDLE

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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
Syringe: suspension
Needles
50 x 1 dose
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/008

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING PACK SIZE OF 1 VIAL WITH BIOSET® AND 1 PREFILLED SYRINGE WITHOUT NEEDLE

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 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
Pertussis antigens	
(Pertussis toxoid[1], Filamentous haemagglutinin[1], Pertactin[1])	25, 25, 8 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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 with Bioset® Cap: powder
Syringe: suspension
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/009

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING PACK SIZE OF 10 VIALS WITH BIOSET® AND 10 PREFILLED SYRINGES WITHOUT NEEDLE

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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 with Bioset® Cap: powder
Syringe: suspension
10 x 1 dose
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/010

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING PACK SIZE OF 20 VIALS WITH BIOSET® AND 20 PREFILLED SYRINGES WITHOUT NEEDLE

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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 with Bioset® Cap: powder
Syringe: suspension
20 x 1 dose
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/011

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING PACK SIZE OF 50 VIALS WITH BIOSET® AND 50 PREFILLED SYRINGES WITHOUT NEEDLE

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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 with Bioset® Cap: powder
Syringe: suspension
50 x 1 dose
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/012

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
PACK SIZE OF 1 VIAL WITH BIOSET® AND 1 PREFILLED SYRINGE WITH 1 NEEDLE

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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 with Bioset® Cap: powder
Syringe: suspension
Needle
1 dose (0.5 ml):

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/013

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING PACK SIZE OF 10 VIALS WITH BIOSET® AND 10 PREFILLED SYRINGES WITH 1 NEEDLE

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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 with Bioset® Cap: powder
Syringe: suspension
Needle
10 x 1 dose
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/014

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING PACK SIZE OF 20 VIALS WITH BIOSET® AND 20 PREFILLED SYRINGES WITH 1 NEEDLE

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* 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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 with Bioset® Cap: powder
Syringe: suspension
Needle
20 x 1 dose
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/015

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING PACK SIZE OF 50 VIALS WITH BIOSET® AND 50 PREFILLED SYRINGES WITH 1 NEEDLE

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* 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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 with Bioset® Cap: powder
Syringe: suspension
Needle
50 x 1 dose
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/016

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING PACK SIZE OF 1 VIAL WITH BIOSET® AND 1 PREFILLED SYRINGE WITH 2 NEEDLES

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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 with Bioset® Cap: powder
Syringe: suspension
Needles
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/017

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

PARTICULARS TO APPEAR ON THE OUTER PACKAGING PACK SIZE OF 10 VIALS WITH BIOSET® AND 10 PREFILLED SYRINGES WITH 2 NEEDLES

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 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 µg
Hepatitis B surface antigen[2,3]	10 µg
Poliovirus (inactivated) type 1, 2, 3	40, 8, 32 DU
Haemophilus type b polysaccharide (polyribosylribitol phosphate)[3] conjugated to tetanus toxoid as carrier protein	10 µg 20-40 µg

[1]adsorbed on $Al(OH)_3$ 0.95 mg Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on $AlPO_4$ 1.45 mg Al^{3+}

3. LIST OF EXCIPIENTS

Lactose anhydrous
NaCl
phenoxyethanol (2.5 mg)
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 with Bioset® Cap: powder
Syringe: suspension
Needles
10 x 1 dose
1 dose (0.5 ml)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

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/1/00/152/018

13. BATCH NUMBER

LOT:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

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

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

HIB for Infanrix hexa
Powder and 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

6. OTHER

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

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

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

Read all of this leaflet carefully before your child starts receiving this vaccine.
- Keep this leaflet until your child has finished the complete vaccination course. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- This vaccine has been prescribed for your child. Do not pass it on to others.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT Infanrix hexa IS AND WHAT IT IS USED FOR

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code J07CA

Infanrix hexa is a vaccine used in children to prevent six diseases: diphtheria, tetanus (lockjaw), pertussis (whooping cough), hepatitis B, poliomyelitis (Polio) and *Haemophilus influenzae* type b. The vaccine works by causing the body to produce its own protection (antibodies) against these diseases.

- **Diphtheria:** Diphtheria mainly affects the airways and sometimes the skin. Generally the airways become inflamed (swollen) causing severe breathing difficulties and sometimes suffocation. The bacteria also release a toxin (poison), which can cause nerve damage, heart problems, and even death.

- **Tetanus** (Lockjaw): Tetanus bacteria enter the body through cuts, scratches or wounds in the skin. Wounds that are especially prone to infection are burns, fractures, deep wounds or wounds contaminated with soil, dust, horse manure/dung or wood splinters. The bacteria release a toxin (poison), which 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.

- **Pertussis** (Whooping cough): Pertussis is a highly infectious illness. The disease affects the airways causing severe spells of coughing that may interfere with normal breathing. The coughing is often accompanied by a "whooping" sound, hence the common name "whooping cough". The cough may last for 1-2 months or longer. Pertussis can also cause ear infections, bronchitis which may last a long time, pneumonia, fits, brain damage and even death.

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

- **Poliomyelitis (Polio):** Poliomyelitis, sometimes called simply "polio" is a viral infection that can have variable effects. Often it causes only a mild illness but in some people it causes permanent damage or even death. In its severest form, polio infection causes paralysis of the muscles (muscles

cannot move), including those muscles needed for breathing and walking. The limbs affected by the disease may be painfully deformed.

- ***Haemophilus influenzae* type b** (Hib): Hib infection most frequently causes brain inflammation (swelling). There will be some type of serious complications such as: mental retardation, cerebral palsy, deafness, epilepsy or partial blindness. Hib infection also causes inflammation of the throat. It occasionally causes death by suffocation. Less commonly, the bacteria can also infect the blood, heart, lungs, bones, joints, and tissues of the eyes and mouth.

Vaccination is the best way to protect against these diseases. None of the components in the vaccine are infectious.

2. BEFORE YOUR CHILD RECEIVES Infanrix hexa

Infanrix hexa should not be given:

- if your child has previously had any allergic reaction to Infanrix hexa, or any ingredient contained in this vaccine. The active substances and other ingredients in Infanrix hexa are listed at the end of the leaflet. Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue.
- if your child has previously had an allergic reaction to any vaccine against diphtheria, tetanus, pertussis (whooping cough), hepatitis B, poliomyelitis or *Haemophilus influenzae* type b diseases.
- if your child experienced problems of the nervous system within 7 days after previous vaccination with a vaccine against pertussis (whooping cough) disease.
- 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.

Take special care with Infanrix hexa:

- if after previously having Infanrix hexa or another vaccine against pertussis (whooping cough) disease, 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
  - ♦ Seizures/fits with or without a high temperature within 3 days of vaccination
- if your child has a bleeding problem or bruises easily
- if your child has a tendency to seizures/fits due to a fever, or if there is a history in the family of this

Using other medicines or vaccines
Please tell your doctor if your child is taking or has recently taken any other medicines, including medicines obtained without a prescription or has recently received any other vaccine.

Important information about some of the ingredients of Infanrix hexa
Please tell your doctor if your child has had an allergic reaction to neomycin and polymyxin (antibiotics).

3. HOW Infanrix hexa IS GIVEN

Your child will receive a total of three injections with an interval of at least one month between each one. Each injection is given on a separate visit. You will be informed by the doctor or nurse when you should come back for subsequent injections.

If additional injections or "booster" are necessary, the doctor will tell you.

If your child misses a scheduled injection, talk to your doctor and arrange another visit.

Make sure your child finishes the complete vaccination course of three injections. If not, your child may not be fully protected against the diseases.

The doctor will give Infanrix hexa as an injection into the muscle.

The vaccine should never be given into a vein.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Infanrix hexa can cause side effects, although not everybody gets them.

Your child may feel:
- pain or discomfort at the injection site

or you may see some:
- redness or swelling at the injection site.

However, these effects usually clear up within a few days.

Other side effects which can occur are:
- loss of appetite
- fever (more than 38°C)
- sleepiness, irritability, abnormal crying, restlessness

If these events continue or become severe, tell your doctor.

As with all injectable vaccines, there is an extremely small risk of allergic reactions. These can be recognised by:
- Itchy rash of the hands and feet
- Swelling of the eyes and face
- Difficulty in breathing or swallowing
  Such reactions will usually occur before leaving the doctor's surgery. However, you should seek immediate treatment in any event.

Additional side effects that have been reported very rarely (less than 1 per 10,000 doses of vaccine) in the days after vaccination with Infanrix hexa include:
- Collapse or periods of unconsciousness or lack of awareness
- Seizures or fits
- A hard lump at the site of injection
- Diffuse swelling of the entire injected limb

Bleeding or bruising more easily than normal has occurred very rarely with hepatitis B containing vaccines.

Do not be alarmed by this list of possible side effects. It is possible that your child has no side effects from vaccination.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE Infanrix hexa

Keep out of the reach and sight of children.

Do not use Infanrix hexa 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.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Infanrix hexa contains

- The active substances are:

Diphtheria toxoid[1]	not less than 30 IU
Tetanus toxoid[1]	not less than 40 IU
Bordetella pertussis antigens	
Pertussis toxoid[1]	25 micrograms
Filamentous Haemagglutinin[1]	25 micrograms
Pertactin[1]	8 micrograms
Hepatitis B surface antigen[2,3]	10 micrograms
Poliovirus (inactivated)	
type 1 (Mahoney strain)	40 D-antigen unit
type 2 (MEF-1 strain)	8 D-antigen unit
type 3 (Saukett strain)	32 D-antigen unit
Haemophilus type b polysaccharide (polyribosylribitol phosphate) [3] conjugated to tetanus toxoid as carrier protein	10 micrograms 20-40 micrograms

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.95 milligrams Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on aluminium phosphate ($AlPO_4$) 1.45 milligrams Al^{3+}

- The other ingredients in Infanrix hexa are:
  Hib powder: lactose anhydrous

  DTPa-HBV-IPV suspension: sodium chloride (NaCl), phenoxyethanol (2.5 mg), medium 199 containing principally amino acids, mineral salts, vitamins and water for injections

What Infanrix hexa looks like and contents of the pack

Powder and suspension for suspension for injection.

The diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis (DTPa-HBV-IPV) component is a white, slightly milky liquid presented in a prefilled syringe (0.5 ml).

The Hib component is a white powder presented in a glass vial.

Both components must be mixed together before your child receives the vaccine. 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.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last approved in

Detailed information on this medicine is available on the European Medicines Agency (EMEA) web site: http://www.emea.eu.int/.

The following information is intended for medical or healthcare professionals only:

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

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

The DTPa-HBV-IPV suspension should be inspected visually for any foreign particulate matter and/or variation of physical aspect. In the event of either being observed, discard the container.

The vaccine is reconstituted by adding the contents of the syringe to the vial containing the Hib powder. The mixture should then be well shaken until the powder is completely dissolved.

The reconstituted vaccine presents as a slightly more cloudy suspension than the liquid component alone. This is normal and does not impair the performance of the vaccine. In the event of other variation being observed, discard the vaccine.

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 type b (HIB) conjugate vaccine (adsorbed).

Read all of this leaflet carefully before your child starts receiving this vaccine.
- Keep this leaflet until your child has finished the complete vaccination course. You may need to read it again.
- If you have any further questions, ask your doctor or your pharmacist.
- This vaccine has been prescribed for your child. Do not pass it on to others.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT Infanrix hexa IS AND WHAT IT IS USED FOR

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code J07CA

Infanrix hexa is a vaccine used in children to prevent six diseases: diphtheria, tetanus (lockjaw), pertussis (whooping cough), hepatitis B, poliomyelitis (Polio) and *Haemophilus influenzae* type b. The vaccine works by causing the body to produce its own protection (antibodies) against these diseases.

- **Diphtheria:** Diphtheria mainly affects the airways and sometimes the skin. Generally the airways become inflamed (swollen) causing severe breathing difficulties and sometimes suffocation. The bacteria also release a toxin (poison), which can cause nerve damage, heart problems, and even death.

- **Tetanus** (Lockjaw): Tetanus bacteria enter the body through cuts, scratches or wounds in the skin. Wounds that are especially prone to infection are burns, fractures, deep wounds or wounds contaminated with soil, dust, horse manure/dung or wood splinters. The bacteria release a toxin (poison), which 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.

- **Pertussis** (Whooping cough): Pertussis is a highly infectious illness. The disease affects the airways causing severe spells of coughing that may interfere with normal breathing. The coughing is often accompanied by a "whooping" sound, hence the common name "whooping cough". The cough may last for 1-2 months or longer. Pertussis can also cause ear infections, bronchitis which may last a long time, pneumonia, fits, brain damage and even death.

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

- **Poliomyelitis (Polio):** Poliomyelitis, sometimes called simply "polio" is a viral infection that can have variable effects. Often it causes only a mild illness but in some people it causes permanent damage or even death. In its severest form, polio infection causes paralysis of the muscles (muscles

cannot move), including those muscles needed for breathing and walking. The limbs affected by the disease may be painfully deformed.

- ***Haemophilus influenzae* type b (Hib)**: Hib infection most frequently causes brain inflammation (swelling). There will be some type of serious complications such as: mental retardation, cerebral palsy, deafness, epilepsy or partial blindness. Hib infection also causes inflammation of the throat. It occasionally causes death by suffocation. Less commonly, the bacteria can also infect the blood, heart, lungs, bones, joints, and tissues of the eyes and mouth.

Vaccination is the best way to protect against these diseases. None of the components in the vaccine are infectious.

2. BEFORE YOUR CHILD RECEIVES Infanrix hexa

Infanrix hexa should not be given:

- if your child has previously had any allergic reaction to Infanrix hexa, or any ingredient contained in this vaccine. The active substances and other ingredients in Infanrix hexa are listed at the end of the leaflet. Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue.
- if your child has previously had an allergic reaction to any vaccine against diphtheria, tetanus, pertussis (whooping cough), hepatitis B, poliomyelitis or *Haemophilus influenzae* type b diseases.
- if your child experienced problems of the nervous system within 7 days after previous vaccination with a vaccine against pertussis (whooping cough) disease.
- 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.

Take special care with Infanrix hexa:

- if after previously having Infanrix hexa or another vaccine against pertussis (whooping cough) disease, 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
  - ♦ Seizures/fits with or without a high temperature within 3 days of vaccination
- if your child has a bleeding problem or bruises easily
- if your child has a tendency to seizures/fits due to a fever, or if there is a history in the family of this

Using other medicines or vaccines
Please tell your doctor if your child is taking or has recently taken any other medicines, including medicines obtained without a prescription or has recently received any other vaccine.

Important information about some of the ingredients of Infanrix hexa
Please tell your doctor if your child has had an allergic reaction to neomycin and polymyxin (antibiotics).

3. HOW Infanrix hexa IS GIVEN

Your child will receive a total of three injections with an interval of at least one month between each one. Each injection is given on a separate visit. You will be informed by the doctor or nurse when you should come back for subsequent injections.

If additional injections or "booster" are necessary, the doctor will tell you.

If your child misses a scheduled injection, talk to your doctor and arrange another visit.

Make sure your child finishes the complete vaccination course of three injections. If not, your child may not be fully protected against the diseases.

The doctor will give Infanrix hexa as an injection into the muscle.

The vaccine should never be given into a vein.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Infanrix hexa can cause side effects, although not everybody gets them.

Your child may feel:
- pain or discomfort at the injection site

or you may see some:
- redness or swelling at the injection site.

However, these effects usually clear up within a few days.

Other side effects which can occur are:
- loss of appetite
- fever (more than 38°C)
- sleepiness, irritability, abnormal crying, restlessness

If these events continue or become severe, tell your doctor.

As with all injectable vaccines, there is an extremely small risk of allergic reactions. These can be recognised by:
- Itchy rash of the hands and feet
- Swelling of the eyes and face
- Difficulty in breathing or swallowing
  Such reactions will usually occur before leaving the doctor's surgery. However, you should seek immediate treatment in any event.

Additional side effects that have been reported very rarely (less than 1 per 10,000 doses of vaccine) in the days after vaccination with Infanrix hexa include:
- Collapse or periods of unconsciousness or lack of awareness
- Seizures or fits
- A hard lump at the site of injection
- Diffuse swelling of the entire injected limb

Bleeding or bruising more easily than normal has occurred very rarely with hepatitis B containing vaccines.

Do not be alarmed by this list of possible side effects. It is possible that your child has no side effects from vaccination.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE Infanrix hexa

Keep out of the reach and sight of children.

Do not use Infanrix hexa 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.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Infanrix hexa contains

- The active substances are:

Diphtheria toxoid[1]	not less than 30 IU
Tetanus toxoid[1]	not less than 40 IU
Bordetella pertussis antigens	
Pertussis toxoid[1]	25 micrograms
Filamentous Haemagglutinin[1]	25 micrograms
Pertactin[1]	8 micrograms
Hepatitis B surface antigen[2,3]	10 micrograms
Poliovirus (inactivated)	
type 1 (Mahoney strain)	40 D-antigen unit
type 2 (MEF-1 strain)	8 D-antigen unit
type 3 (Saukett strain)	32 D-antigen unit
Haemophilus type b polysaccharide (polyribosylribitol phosphate) [3] conjugated to tetanus toxoid as carrier protein	10 micrograms 20-40 micrograms

[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$) 0.95 milligrams Al^{3+}
[2]produced in yeast cells (*Saccharomyces cerevisae*) by recombinant DNA technology
[3]adsorbed on aluminium phosphate ($AlPO_4$) 1.45 milligrams Al^{3+}

- The other ingredients in Infanrix hexa are:
  Hib powder: lactose anhydrous

  DTPa-HBV-IPV suspension: sodium chloride (NaCl), phenoxyethanol (2.5 mg), medium 199 containing principally amino acids, mineral salts, vitamins and water for injections

What Infanrix hexa looks like and contents of the pack

Powder and suspension for suspension for injection.

The diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis (DTPa-HBV-IPV) component is a white, slightly milky liquid presented in a prefilled syringe (0.5 ml).

The Hib component is a white powder presented in a glass vial with Bioset®.

Both components must be mixed together before your child receives the vaccine. 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.

Not all pack sizes may be marketed.

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This leaflet was last approved in

Detailed information on this medicine is available on the European Medicines Agency (EMEA) web site: http://www.emea.eu.int/.

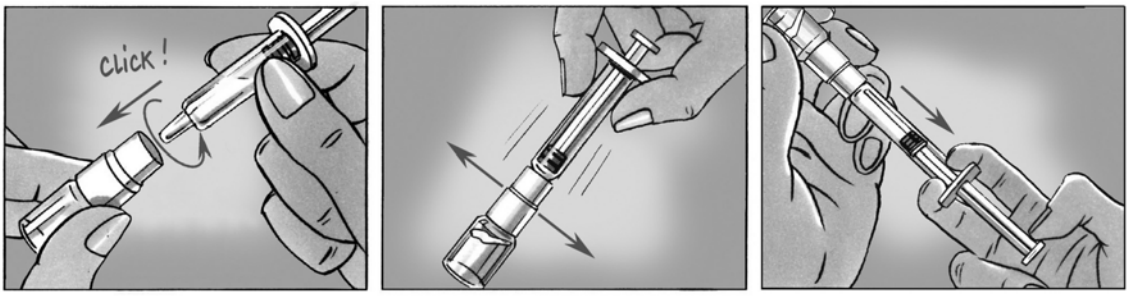
The following information is intended for medical or healthcare professionals only:

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

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

The DTPa-HBV-IPV suspension should be inspected visually for any foreign particulate matter and/or variation of physical aspect. In the event of either being observed, discard the container.

The Bioset® is a specially designed cap which simplifies reconstitution. It is good clinical practice to only inject a vaccine when it has reached room temperature. In addition, a vial at room temperature ensures sufficient elasticity of the rubber closure to minimise any coring of rubber particles. To achieve this, the vial should be kept at room temperature (25 ± 3 °C) for at least five minutes before connecting the syringe and reconstituting the vaccine. For reconstitution, twist the cover from the Bioset® cap and remove the cap from the syringe. Before connecting the syringe onto the Bioset®, make sure the two containers are aligned (see Picture 1). Connect the syringe onto the Bioset® by twisting it. Push downwards until syringe 'clicks' into position. Inject liquid, mix thoroughly until powder is completely dissolved. Aspirate reconstituted vaccine back into syringe. Unscrew syringe from Bioset®. Affix a needle for administration.



The reconstituted vaccine presents as a slightly more cloudy suspension than the liquid component alone. This is normal and does not impair the performance of the vaccine. In the event of other variation being observed, discard the vaccine.