# Infanrix hexa

## 1. NAME OF THE MEDICINAL PRODUCT

**Infanrix hexa**

Combined diphtheria-tetanus-acellular pertussis, hepatitis B, enhanced inactivated polio vaccine and *Haemophilus influenzae* type b vaccine.

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (0.5 ml) contains:

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

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

The DTPa-HBV-IPV component is presented as a turbid white suspension. Upon storage, a white deposit and clear supernatant can be observed. This is a normal observation.

The Hib component is presented as a white powder.

For excipients, see section 6.1 List of Excipients.

## 3. PHARMACEUTICAL FORM

Powder and suspension for suspension for injection.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

**Infanrix hexa** is indicated for primary and booster vaccination of infants and toddlers against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and *Haemophilus influenzae* type b.
The use of **Infanrix hexa** should be in accordance with official recommendations.

## 4.2 Posology and Method of Administration

The primary vaccination schedule consists of two or three doses (of 0.5 ml) which should be administered according to official recommendations (see 5.1 Pharmacodynamic Properties for schedules evaluated in clinical trials). **Infanrix hexa** can be considered for the booster if the antigen composition is in accordance with the official recommendations.

| Primary vaccination | Booster vaccination | General considerations |
|---|---|---|
| **Full-term infants** | | |
| 3-dose | A booster dose may be given. | • There should be an interval of at least 1 month between primary doses.<br>• When giving a booster dose, this should be at least 6 months after the last priming dose and preferably before 18 months of age. |
| 2-dose | A booster dose must be given. | • There should be an interval of at least 1 month between primary doses.<br>• When giving a booster dose, this should be at least 6 months after the last priming dose and preferably between 11 and 13 months of age. |
| **Preterm infants born after at least 24 weeks of gestational age** | | |
| 3-dose | A booster dose must be given. | • There should be an interval of at least 1 month between primary doses.<br>• When giving a booster dose, this should be at least 6 months after the last priming dose and preferably before 18 months of age. |

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.

Where a dose of hepatitis B vaccine is given at birth, **Infanrix hexa** can be used as a replacement for supplementary doses of hepatitis B vaccine from the age of 6 weeks. If a second dose of hepatitis B vaccine is required before this age, monovalent hepatitis B vaccine should be used.
Locally established immunoprophylactic measures against hepatitis B should be maintained.

Other combinations of antigens have been studied in clinical trials following primary vaccination with **Infanrix hexa** and may be used for a booster dose: diphtheria, tetanus, acellular pertussis (DTPa), diphtheria, tetanus, acellular pertussis, *Haemophilus influenzae* type b (DTPa+Hib), diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis, *Haemophilus influenzae* type b (DTPa-IPV+Hib) and diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliomyelitis, *Haemophilus influenzae* type b (DTPa-HBV-IPV+Hib).

**Method of administration**
**Infanrix hexa** is for deep intramuscular injection.

## 4.3 Contra-indications

Hypersensitivity to the active substances or to any of the excipients or residues (see section 2 Qualitative and Quantitative Composition and 6.1 List of Excipients).

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

**Infanrix hexa** is contraindicated if the child has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis containing vaccine. In these circumstances pertussis vaccination should be discontinued and the vaccination course should be continued with diphtheria-tetanus, hepatitis B, inactivated polio and Hib vaccines.

**4.4 Special Warnings and Precautions for Use**

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.

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.

A protective immune response may not be elicited in all vaccinees (see 5.1 Pharmacodynamic properties).

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

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 of vaccination, not due to another identifiable cause.
- Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours of vaccination.
- Persistent, inconsolable crying lasting ≥ 3 hours, occurring within 48 hours of vaccination.
- Convulsions with or without fever, occurring within 3 days of vaccination.

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

In children with progressive neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy, it is better to defer pertussis (Pa or Pw) immunisation until the condition is corrected or stable. However, the decision to give pertussis vaccine must be made on an individual basis after careful consideration of the risks and benefits.

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.

**Do not administer the vaccine intravascularly or intradermally.**

A history of febrile convulsions, a family history of convulsions, or Sudden Infant Death Syndrome (SIDS) do not constitute contraindications for the use of **Infanrix hexa**. Vaccinees

with a history of febrile convulsions should be closely followed up as such adverse events may occur within 2 to 3 days post vaccination.

Data from clinical studies indicate that, when **Infanrix hexa** is co-administered with pneumococcal conjugate vaccine, the rate of febrile reactions is higher compared to that occurring following the administration of **Infanrix hexa** alone.

Increased reporting rates of convulsions (with or without fever) and hypotonic hyporesponsive episode (HHE) were observed with concomitant administration of **Infanrix hexa** and Prevenar 13 (see 4.8 Undesirable Effects).

Antipyretic treatment should be initiated according to local treatment guidelines.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

*Special populations*

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

Clinical data indicate that **Infanrix hexa** can be given to preterm infants, however, as expected in this population, a lower immune response has been observed for some antigens (see 4.8 Undesirable Effects and 5.1 Pharmacodynamic Properties).

The potential risk of apnoea and the need for respiratory monitoring for 48-72h should be considered when administering the primary immunisation series to very preterm infants (born ≤28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in these infants, vaccination should not be withheld or delayed.

*Interference with laboratory testing*

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

## 4.5 Interaction with Other Medicinal Products and Other Forms of Interactions

**Infanrix hexa** can be given concomitantly with pneumococcal conjugate, MenC conjugate, MenACWY conjugate, MenB, rotavirus, measles, mumps, rubella and varicella vaccines. Data have shown no clinically relevant interference in the antibody response to each of the individual antigens.

When **Infanrix hexa** was co-administered with MenB and pneumococcal conjugate vaccines, inconsistent results were seen across studies for responses to inactivated poliovirus type 2 and pneumococcal conjugate serotype 6B antigen but these data do not suggest clinically significant interference.

Data from clinical studies indicate that, when **Infanrix hexa** is co-administered with pneumococcal conjugate vaccine, the rate of febrile reactions is higher compared to that occurring following the administration of **Infanrix hexa** alone (see 4.4 Special Warnings and Precautions for Use for guidance on pneumococcal conjugate vaccines).

Data from clinical studies indicate a more frequent occurrence of fever, pain at the injection site, appetite lost and irritability when **Infanrix hexa** is co-administered with MenB vaccine and 7-valent pneumococcal conjugate vaccine.

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

**4.6 Pregnancy and Lactation**

As **Infanrix hexa** is not intended for use in adults, information on the safety of the vaccine when used during pregnancy or lactation is not available.

**4.7 Effects on Ability to Drive and Use Machines**

Not relevant.

**4.8 Undesirable Effects**

*Clinical trials Data:*

The safety profile presented below is based on data from more than 16,000 subjects.

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

Adverse reactions reported are listed according to the following frequency.

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

| System Organ Class | Frequency | Adverse events |
|---|---|---|
| Infections and infestations | Uncommon | upper respiratory tract infection |
| Metabolism and nutrition disorders | Very common | appetite lost |
| Psychiatric disorders | Very common | irritability, crying abnormal, restlessness |
| | Common | nervousness |
| Nervous system disorders | Very common | somnolence |
| | Very rare | convulsions (with or without fever)*** |
| Respiratory, thoracic and mediastinal disorders | Uncommon | cough* |
| | Rare | bronchitis |
| Gastrointestinal disorders | Common | vomiting, diarrhoea |
| Skin and subcutaneous tissue disorders | Common | pruritus* |
| | Rare | rash |
| | Very rare | dermatitis, urticaria* |

| | | |
|---|---|---|
| General disorders and administration site conditions | Very common | pain, redness, local swelling at the injection site (≤ 50 mm), fever ≥ 38°C |
| | Common | local swelling at the injection site (> 50 mm)**, fever >39.5°C, injection site reactions, including induration |
| | Uncommon | diffuse swelling of the injected limb, sometimes involving the adjacent joint**, fatigue |

* observed only with other GSK DTPa-containing vaccines
** 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.
*** Analysis of postmarketing reporting rates suggests a potential increased risk of convulsions (with or without fever) and HHE when comparing groups which reported use of **Infanrix hexa** with Prevnar 13/ Prevenar 13 to those which reported use of **Infanrix hexa** alone.

*Post Marketing Data*
The following drug-related adverse reactions were reported during post-marketing surveillance.

| **System Organ Class** | **Frequency** | **Adverse events** |
|---|---|---|
| Blood and lymphatic system disorders | Rare | Lymphadenopathy, thrombocytopenia |
| Immune system disorders | Rare | Allergic reactions (including anaphylactic and anaphylactoid reactions) |
| Nervous system disorders | Rare | Collapse or shock-like state (hypotonic hyporesponsive episode)*** |
| Respiratory, thoracic and mediastinal disorders | Rare | Apnoea*[see Warnings and Precautions for apnoea in very preterm infants (≤ 28 weeks of gestation)] |
| Skin and subcutaneous tissue disorders | Rare | Angioneurotic oedema* |
| General disorders and administration site conditions | Rare | Extensive swelling reactions, swelling of the entire injected limb**, vesicles at the injection site |

*observed only with other GSK DTPa-containing vaccines.
**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.
*** Analysis of postmarketing reporting rates suggests a potential increased risk of convulsions (with or without fever) and HHE when comparing groups which reported use of **Infanrix hexa** with Prevnar 13/ Prevenar 13 to those which reported use of **Infanrix hexa** alone.

*Safety in preterm infants*

**Infanrix hexa** has been administered to more than 1000 preterm infants (born after a gestation period of 24 to 36 weeks) in primary vaccination studies and in more than 200 preterm infants as a booster dose in the second year of life. In comparative studies, similar rates of symptoms were observed in preterm and full-term infants.

*Safety in infants and toddlers born to mothers vaccinated with dTpa during pregnancy*
In clinical studies, **Infanrix hexa** has been administered to more than 500 subjects born to mothers vaccinated with dTpa or placebo during pregnancy. The safety profile of **Infanrix hexa** was similar regardless of exposure/non-exposure to dTpa during pregnancy.

*Experience with hepatitis B vaccine*
Paralysis, neuropathy, encephalopathy, encephalitis, meningitis, allergic reactions mimicking serum sickness, neuritis, hypotension, vasculitis, lichen planus, erythema multiforme, arthritis and muscular weakness have been reported during post-marketing surveillance following GlaxoSmithKline Biologicals' hepatitis B vaccine in infants and toddlers <2 years old. The causal relationship to the vaccine has not been established.

### 4.9 Overdose
Insufficient data are available.

## 5. PHARMACOLOGICAL PROPERTIES
### 5.1 Pharmacodynamic Properties
Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code J07CA09.

*Immunogenicity*

The immunogenicity of **Infanrix hexa** has been evaluated in clinical studies from 6 weeks of age. The vaccine was assessed in 2-dose and 3-dose priming schedules, including the schedule for the Expanded Program on Immunisation, and as a booster dose. The results of these clinical studies are summarised in the tables below.

After a 3-dose primary vaccination schedule, at least 95.7% of infants had developed seroprotective or seropositive antibody levels against each of the vaccine antigens. After booster vaccination (post-dose 4), at least 98.4% of children had developed seroprotective or seropositive antibody levels against each of the vaccine antigens.

**Percentage of subjects with antibody titres ≥ assay cut-off one month after 3-dose primary and booster vaccination with Infanrix hexa**

| **Antibody (cut-off)** | **Post-dose 3** | | | | **Post-dose 4 (Booster vaccination during the second year of life following a 3-dose primary course)** |
|---|---|---|---|---|---|
| | **2-3-4 months N= 196 (2 studies)** | **2-4-6 months N= 1,693 (6 studies)** | **3-4-5 months N= 1055 (6 studies)** | **6-10-14 weeks N= 265 (1 study)** | **N=2,009 (12 studies)** |
| | **%** | **%** | **%** | **%** | **%** |
| **Anti-diphtheria** (0.1 IU/ml) † | 100.0 | 99.8 | 99.7 | 99.2 | 99.9 |
| **Anti-tetanus** (0.1 IU/ml) † | 100.0 | 100.0 | 100.0 | 99.6 | 99.9 |
| **Anti-PT** (5 EL.U/ml) | 100.0 | 100.0 | 99.8 | 99.6 | 99.9 |
| **Anti-FHA** (5 EL.U/ml) | 100.0 | 100.0 | 100.0 | 100.0 | 99.9 |
| **Anti-PRN** (5 EL.U/ml) | 100.0 | 100.0 | 99.7 | 98.9 | 99.5 |
| **Anti-HBs** (10 mIU/ml) † | 99.5 | 98.9 | 98.0 | 98.5* | 98.4 |
| **Anti-Polio type 1** (1/8 dilution) † | 100.0 | 99.9 | 99.7 | 99.6 | 99.9 |
| **Anti-Polio type 2** (1/8 dilution) † | 97.8 | 99.3 | 98.9 | 95.7 | 99.9 |
| **Anti-Polio type 3** (1/8 dilution) † | 100.0 | 99.7 | 99.7 | 99.6 | 99.9 |
| **Anti-PRP** (0.15 µg/ml) † | 96.4 | 96.6 | 96.8 | 97.4 | 99.7 |

N = number of subjects

* in a subgroup of infants not administered hepatitis B vaccine at birth, 77.7% of subjects had anti-HBs titres ≥ 10 mIU/ml
† cut-off accepted as indicative of protection

After a complete vaccination according to a 2-dose primary and booster schedule with **Infanrix hexa**, at least 97.9% of the subjects had developed seroprotective or seropositive antibody levels against each of the vaccine antigens.

**Percentage of subjects with antibody titres ≥ assay cut-off one month after 2-dose primary and booster vaccination with Infanrix hexa**

| **Antibody (cut-off)** | **Post-dose 3 (Vaccination at 2-4-12 months of age) N=196 (1 study)** | **Post-dose 3 (Vaccination at 3-5-11 months of age) N=532 (3 studies)** |
|---|---|---|
| | **%** | **%** |
| **Anti-diphtheria** (0.1 IU/ml) † | 100.0 | 100.0 |
| **Anti-tetanus** (0.1 IU/ml) † | 100.0 | 100.0 |
| **Anti-PT** (5 EL.U/ml) | 99.5 | 100.0 |
| **Anti-FHA** (5 EL.U/ml) | 100.0 | 100.0 |
| **Anti-PRN** (5 EL.U/ml) | 100.0 | 99.2 |
| **Anti-HBs** (10 mIU/ml) † | 99.8 | 98.9 |
| **Anti-Polio type 1** (1/8 dilution) † | 98.4 | 99.8 |
| **Anti-Polio type 2** (1/8 dilution) † | 98.4 | 99.4 |
| **Anti-Polio type 3** (1/8 dilution) † | 97.9 | 99.2 |
| **Anti-PRP** (0.15 µg/ml) † | 100.0 | 99.6 |

N = number of subjects

† cut-off accepted as indicative of protection

Serological correlates of protection have been established for diphtheria, tetanus, polio, Hepatitis B and Hib. For pertussis there is no serological correlate of protection. However, as the immune response to pertussis antigens following **Infanrix hexa** administration is equivalent to that of **Infanrix** (DTPa), the protective efficacy of the two vaccines is expected to be equivalent.

*Efficacy in protecting against pertussis*

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

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

*Immunogenicity in infants and toddlers born to mothers vaccinated with dTpa during pregnancy*

Clinical data from more than 500 infants and toddlers did not show clinically relevant interference between maternal vaccination with **Boostrix** and the infant and toddler response to diphtheria, tetanus, hepatitis B, inactivated polio virus, *Haemophilus influenzae* type b or pneumococcal antigens. Although lower concentrations of antibodies against some pertussis antigens were observed post primary and post booster vaccination, 92.1-98.1% of subjects born to vaccinated mothers showed a booster response against all pertussis antigens. Current epidemiological data on pertussis disease do not suggest any clinical relevance of this immune interference.

*Immunogenicity in preterm infants*

The immunogenicity of **Infanrix hexa** was evaluated across three studies including approximately 300 preterm infants (born after a gestation period of 24 to 36 weeks) following a 3-dose primary vaccination course at 2, 4 and 6 months of age. The immunogenicity of a booster dose at 18 to 24 months of age was evaluated in approximately 200 preterm infants.

One month after primary vaccination at least 98.7% of subjects were seroprotected against diphtheria, tetanus and poliovirus types 1 and 2; at least 90.9% had seroprotective antibody levels against the hepatitis B, PRP and poliovirus type 3 antigens; and all subjects were seropositive for antibodies against FHA and PRN while 94.9% were seropositive for anti-PT antibodies.

One month after the booster dose at least 98.4% of subjects had seroprotective or seropositive antibody levels against each of the antigens except against PT (at least 96.8%) and hepatitis B (at least 88.7%). The response to the booster dose in terms of fold increases in antibody concentrations (15- to 235-fold), indicate that preterm infants were adequately primed for all the antigens of **Infanrix hexa**.

In a follow-up study, approximately 2.5 to 3 years after the booster dose, 85.3% of the children were still seroprotected against hepatitis B and at least 95.7% were seroprotected against the three poliovirus types and PRP.

*Persistence of the immune response*

The persistence of the immune response to a 3-dose primary and booster schedule with **Infanrix hexa** was evaluated in children 4-8 years of age. Protective immunity against the three poliovirus types and PRP was observed in at least 91.0% of children and against diphtheria and tetanus in at least 64.7% of children. At least 25.4% (anti-PT), 97.5% (anti-FHA) and 87.0% (anti-PRN) of children were seropositive against the pertussis components.

With regards to hepatitis B, seroprotective antibody concentrations following a 3-dose primary and booster schedule with **Infanrix hexa** has been shown to persist in ≥85% of subjects 4-5 years of age , in ≥72% of subjects 7-8 years of age and in ≥60% of subjects 12-13 years of age and in 53.7% of subjects 14-15 years of age. Additionally, following a 2-dose primary and booster schedule, seroprotective antibody concentrations against hepatitis B persisted in ≥48% of subjects 11-12 years of age.

Hepatitis B immunological memory was confirmed in children 4 to 15 years of age. These children had received **Infanrix hexa** as primary and booster vaccination in infancy, and when an additional dose of monovalent HBV vaccine was administered, protective immunity was induced in at least 93% of subjects.

*Post marketing experience*

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

The effectiveness of the Hib component of **Infanrix hexa** was investigated via an extensive post-marketing surveillance study conducted in Germany. Over a seven year follow-up period, the effectiveness of the Hib components of two hexavalent vaccines, of which one was **Infanrix hexa**, was 89.6% for a full primary series and 100% for a full primary series plus booster dose (irrespective of the Hib vaccine used for priming).

**Infanrix hexa** has been the principal Hib-containing vaccine available in Italy since 2006. The vaccine is administered at 3, 5 and 11 months of age and coverage has exceeded 95%. Hib disease has continued to be well controlled, with no more than three confirmed Hib cases reported annually between 2006 and 2011 in Italian children aged less than 5 years.

## 5.2 Pharmacokinetic Properties

Evaluation of pharmacokinetic properties is not required for vaccines.

## Clinical Studies

See section 5.1 Pharmacodynamic Properties.

## 5.3 Preclinical Safety Data

Preclinical 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 Excipient

Lactose, sodium chloride (NaCl), Medium 199 (as stabilizer containing amino acids, mineral salts and vitamins), water for injections.
Neomycin sulphate and polymyxin B sulphate are present as residuals from the manufacturing process.

## 6.2 Incompatibilities

**Infanrix hexa** should not be mixed with other vaccines in the same syringe.

## 6.3 Shelf Life

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

## 6.4 Special Precautions for Storage

Store in a refrigerator (2°C - 8°C).
**The DTPa-HBV-IPV suspension and the reconstituted vaccine must not be frozen. Discard if they have been frozen.**
Protect from light.

During transport, recommended conditions of storage must be respected.

Stability data indicate that the vaccine components are stable at temperatures up to 25°C for 72 hours. These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

The storage conditions are detailed on the packaging.

## 6.5 Nature and Contents of Container

The DTPa-HBV-IPV component is presented in a pre-filled syringe.
The Hib component is presented in a glass vial.
Powder in a vial (type I glass) containing 1 dose with a stopper (butyl rubber) and 0.5 ml of suspension in a pre-filled syringe (type I glass) with a plunger stopper (butyl rubber) and with a rubber tip cap.
The tip cap and rubber plunger stopper of the pre-filled syringe and the stopper of the vial are not made with natural rubber latex.
Pack sizes of 1, 10 and 50, with or without needles.
Not all presentations are available in every country.

## 6.6 Instructions for Use and Handling

The DTPa-HBV-IPV suspension should be well shaken in order to obtain a homogeneous turbid white suspension. The DTPa-HBV-IPV suspension and the Hib powder should be inspected visually for any foreign particulate matter and/or variation of physical aspect. In the event of either being observed, do not administer the vaccine.

**Infanrix hexa** must be reconstituted by adding the entire content of the pre-filled syringe to the vial containing the Hib powder. The mixture should be well shaken until the powder is completely dissolved in the suspension.

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 minimize 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 pre-filled syringe and reconstituting the vaccine.

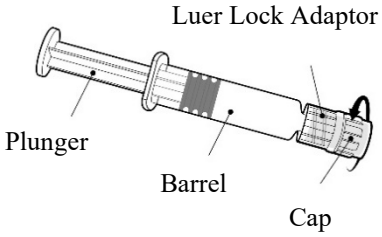
The reconstituted vaccine presents as a slightly more cloudy suspension than the liquid component alone. This is a normal observation.

The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or abnormal physical appearance. In the event of either being observed, do not administer the vaccine.

**After reconstitution, the vaccine should be injected immediately. However the vaccine may be kept for up to 8 hours at room temperature (21°C).**

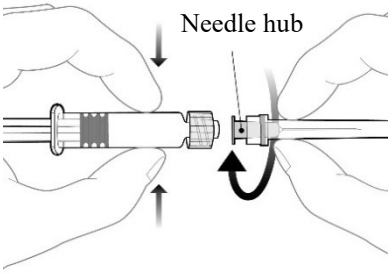
Withdraw the entire contents of the vial.

Instructions for the pre-filled syringe




Hold the syringe by the barrel, not by the plunger.

Unscrew the syringe cap by twisting it anticlockwise.




To attach the needle, connect the hub to the Luer Lock Adaptor and rotate a quarter turn clockwise until you feel it lock.

Do not pull the syringe plunger out of the barrel. If it happens, do not administer the vaccine.

Disposal

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

## 7. MARKETING AUTHORIZATION HOLDER

GlaxoSmithKline (Thailand) Ltd.

## 8. MARKETING AUTHORIZATION NUMBER

2C 16/45 (N)

## 9. DATE OF AUTHORIZATION

13 Sep 2002 (conditional license)
25 May 2005 (unconditional license)

Date of revision of text: 03 October 2023



| |
|---|
| **Version number: GDS22/IPI17 / Date of issue: 12/08/2022**<br>**© 2023 GSK Group of Companies** |
| **Manufacturer:**<br>**GlaxoSmithKline Biologicals s.a.**<br>**89, rue de l'Institut - 1330 Rixensart**<br>**Belgium**<br>**Tel: (32) 2 656 81 11** |

INFANRIX HEXA IM 17.0 TH