For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

INFANRIX

Diphtheria, Tetanus and Pertussis (Acellular, Component) Vaccine (Adsorbed) Ph. Eur.

1. NAME OF THE MEDICINAL PRODUCT

Diphtheria, Tetanus and Pertussis (Acellular, Component) Vaccine (Adsorbed) Ph. Eur.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 mL) contains:

Diphtheria toxoid (D) ----------≥30 IU
Tetanus toxoid (T)----------≥40 IU

Bordetella pertussis antigens (Pa):
Pertussis toxoid ----------25 micrograms
Filamentous haemagglutinin-------25 micrograms
Pertactin----------8 micrograms

Adsorbed aluminium hydroxide----------0.5 mg Al

This vaccine may contain traces of formaldehyde, which was used during the manufacturing process (see section *4.3 Contraindications*).

For a full list of excipients, see Section *6.1 List of Excipients.*

3. PHARMACEUTICAL FORM

Suspension for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

INFANRIX is indicated for active primary immunization against diphtheria, tetanus, and pertussis, in children from the age of 2 months and above, or as a booster dose for children previously immunised with three or four doses of either diphtheria, tetanus and acellular pertussis (DTPa) vaccine or diphtheria, tetanus and whole-cell pertussis (DTPw) vaccine.

4.2 Posology and method of administration

Posology

The recommended dose (0.5 ml) of the vaccine should be administered according to the official vaccination schedule.

The primary immunization course consists of 3 doses with boosters during the second and sixth year of life.

Method of administration

The injection is administered intramuscularly in the anterolateral side of the thigh.

INFANRIX should be administered with caution to subjects with thrombocytopenia or a coagulation disorder, since bleeding may occur during intramuscular administration to these subjects. Firm pressure should be applied to the injection site (without rubbing) for at least 2 minutes.

4.3 Contraindications

INFANRIX is contraindicated in children with known hypersensitivity to the active substances in this vaccine or to any of the excipients listed in section *6.1 List of Excipients*, or to formaldehyde, or those having shown signs of hypersensitivity after previous administration of *INFANRIX* or a whole-cell diphtheria, tetanus and pertussis vaccine or a diphtheria and/or tetanus vaccine.

INFANRIX is contra-indicated in children having experienced encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis containing vaccine. In these circumstances the vaccination course should be continued with diphtheria and tetanus vaccine.

As with other vaccines, the administration of *INFANRIX* should be postponed for acute febrile illnesses. The presence of a minor infection, however, is not a contraindication.

INFANRIX should no longer be administered after the age of 7 years; the dose of diphtheria toxoid is to be decreased at this age.

4.4 Special warnings and precautions for use

It is recommended to review the child's medical history (especially with regard to any undesirable effects that have occurred during previous vaccination) and to carry out a clinical examination prior to vaccination.

Should any of the events listed below occur in temporal relation to receipt of an acellular or whole-cell DTP vaccine, the decision to administer subsequent doses of the vaccine containing the pertussis component should be carefully considered in light of the risks and the expected benefits. There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks, particularly since these events are not associated with permanent sequelae.

The following events were previously considered contraindications for DTPw and can now be considered general precautions after administration of *INFANRIX*:

- Temperature of ≥ 40.5 °C within 48 hours following vaccination, and for which no other cause has been identified.
- Collapse or shock-like state (hypotonic-hyporesponsive episode) occurring within 48 hours of vaccination.
- Persistent and inconsolable crying lasting ≥ 3 hours and occurring within 48 hours of vaccination.
- Convulsions with or without fever, occurring within 3 days of vaccination.

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.

As for any vaccination, the risk/benefit ratio of *INFANRIX* vaccination or deferral should be carefully evaluated in an infant or child suffering from a new onset or progression of a severe neurological disorder.

A history of febrile convulsions and a family history of convulsive fits do not constitute a contra-indication to vaccination with *INFANRIX*.

HIV infection is not considered as a contra-indication.

As with all injectable vaccines, it is advisable to have a solution of adrenaline readily available for injection in the event of possible anaphylactic reaction (see below for emergency treatment). It is generally advisable to keep the vaccinee under medical supervision for 30 minutes following vaccination.

As for all diphtheria, tetanus and pertussis vaccines, the vaccine is to be administered via deep intramuscular injection, preferably at alternate injection sites.

***INFANRIX* should under no circumstances be administered intravenously.**

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

This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially sodium-free.

4.5 Interaction with other medicinal products and other forms of interaction

INFANRIX may be administered at the same time as other paediatric vaccines; however, a measles vaccine (monovalent or combined) is to be administered either concomitantly or at an interval of 1 month.

Different injectable vaccines should always be administered at different injection sites, except *HIBERIX* or *Act-Hib* (Sanofi Pasteur) which can be mixed with *INFANRIX* in the same syringe.

In patients receiving immunosuppressive therapy or patients with immunodeficiency an adequate immunologic response may not be achieved.

4.6 Pregnancy and lactation

INFANRIX is not intended for use in adults, adequate human data on use during pregnancy and adequate animal reproduction studies are not available.

4.7 Effects on ability to drive and use machines

INFANRIX is not intended for use in adults.

4.8 Undesirable effects

Clinical trials:

The safety profile presented below is based on data collected in 20 clinical studies on 11,469 subjects who had received 18,420 doses of the vaccine.

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

The frequencies are as follows:

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

Blood and lymphatic system disorders:
Very rare: lymphadenopathy(1)

Metabolism and nutrition disorders
Common: loss of appetite(2)

Psychiatric conditions
Very common: irritability
Common: restlessness(2), abnormal crying

Nervous system disorders:
Very common: somnolence
Uncommon: headache(1)

Respiratory, thoracic and mediastinal disorders
Uncommon: cough(1), bronchitis(1)

Gastrointestinal disorders
Common: gastrointestinal disorders such as diarrhoea and vomiting

Skin and subcutaneous tissue disorders
Common: pruritus
Uncommon: rash
Rare: urticaria

General disorders and administration site conditions:
Very common: redness, local swelling at the injection site (≤50 mm), fever ≥38.0° C
Common: pain[(2)], local swelling at the injection site (>50 mm)[(3)]
Uncommon: injection site reactions including indurations, fatigue[(1)], fever ≥39.1° C, diffuse swelling of the injected limb, sometimes involving the adjacent joint[(3)].

Post marketing surveillance

Blood and lymphatic system disorders:
Thrombocytopenia[(4)]

Immunity system disorders:
Allergic reactions, including anaphylactic and anaphylactoid reactions

Nervous system disorders:
Shock or shock-like state (hypotonic/hyporesponsive episodes), convulsions (with or without fever) within 2 to 3 days after vaccination.

Respiratory thoracic and mediastinal disorders
Apnoea in very premature infants (≤28 weeks of gestation), see section *4.4 Special warnings and precautions for use*.

Skin and subcutaneous tissue disorders
Angioneurotic oedema

General disorders and administration site conditions:
Swelling of the entire injected limb[(3)]

(1) Reported only with booster vaccination
(2) Very common for booster vaccination
(3) 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. Local swelling at the injection site (>50 mm) and diffuse swelling occur more frequently (very common and common, respectively) during the booster vaccination administered between 4 and 6 years. These reactions resolve over an average of 4 days.
(4) Reported with the D and T vaccines.

4.9 Overdose

Cases of overdose have been reported during post-marketing surveillance. Adverse events, when reported, are not specific but similar to adverse events reported with normal vaccine administration.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Bacterial vaccine: code ATC J07AJ52.

Immune response of *INFANRIX* primary vaccination

One month after the primary vaccination (3 doses administered before the age of 6 months), more than 99 % of infants vaccinated with *INFANRIX* had antibodies titers of more than 0.1 IU/ml to both diphtheria and tetanus.

INFANRIX contains three antigens of the pertussis bacillus, which are considered as important for providing protection against this illness, with the immune response to these three antigens being seen to reach 95 % in clinical trials.

Immune response after the fourth dose of *INFANRIX*

After the administration of a fourth dose between 13 and 24 months, all infants who had already been primed with the first three doses of *INFANRIX* were seen to have antibody titers of more than 0.1 IU/ml to both diphtheria and tetanus, with an immune response to the three pertussis bacillus antigens being observed in more than 96% of these children.

Protective efficacy of *INFANRIX*

The protective efficacy of primary *INFANRIX* vaccination against typical pertussis (as defined by the World Health Organization) was assessed within the context of a prospective blind household contact study carried out until the administration of the fourth dose in infants living in secondary contact with families with children with pertussis.

Based on the data collected during this study, the effective protection afforded by *INFANRIX* reached 88.7%, with a bilateral confidence interval of 95%, from 76.6% to 94.6%.

5.2 Pharmacokinetic properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.3 Preclinical safety data

Non-clinical data from conventional studies of safety and toxicity reveal no specific hazard for humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride, water for injections.

For adsorbent, see section *2. Qualitative and quantitative composition*

6.2 Incompatibilities

INFANRIX should not be mixed with other vaccines in the same syringe, except those mentioned in section 6.6 *Special precautions for disposal and other handling.*

6.3 Shelf life

36 months.

The expiry date is indicated in the label and packaging.

6.4 Special precautions for storage

- Store in a refrigerator between +2°C and +8°C.
- Do not freeze. Destroy the vaccine if it has been frozen.
- Upon removal from refrigerator, the vaccine is stable for 8 hours at 21°C.
- Protect from light.
- Keep out of reach of children.

6.5 Nature and contents of container

0.5 ml suspension for injection in pre-filled syringe (type I glass), fitted with a plunger stopper.

Box of 1 or 10 syringes.

All pack presentations may not be marketed in the country.

6.6 Special precautions for disposal and other handling

- *INFANRIX* is presented as a turbid white suspension in a glass prefilled syringe.
- Upon storage a white deposit and clear supernatant is observed.
- Prior to administration, the vaccine should reach room temperature and be shaken well to obtain a homogenous, turbid white suspension. The vaccine should be inspected visually before administration to detect any foreign particulate matter and/or change in the physical appearance. In the event of either being observed, discard the vaccine.
- If *INFANRIX* vaccine is used for reconstitution of *HIBERIX* or *Act-Hib* vaccine, the entire contents of the *INFANRIX* syringe should be added to the *HIBERIX* or *Act-Hib* vial. In such a case, the diluent supplied in the *HIBERIX* or *Act-Hib* vaccine package must be discarded as it is replaced by the *INFANRIX* vaccine. Once the *INFANRIX* has been added to *HIBERIX* or *Act-Hib*, the mixture should be shaken well. The combined vaccine has a whitish and slightly more opalescent appearance than *INFANRIX* alone. If another variation in appearance is observed, do not use the combined vaccine. After reconstitution of *HIBERIX* or *Act-Hib* with *INFANRIX*, the vaccine must be administered immediately intramuscularly in the anterolateral side of the thigh.

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

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Pharmaceuticals Limited.
Registered office
Dr. Annie Besant Road, Worli
Mumbai 400 030, India.

8. MARKETING AUTHORISATION NUMBER(S)

Import Permission No.: Import - 6175/05

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 23-Sep-2005

Version IFX/PI/IN/2022/01 dated 09-Aug-2022.

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