

# DATA SHEET

## **NAME OF MEDICINAL PRODUCT**

INFANRIX® -IPV

Combined diphtheria-tetanus-acellular pertussis, and enhanced inactivated polio vaccine.

## **PRESENTATION**

INFANRIX®-IPV contains diphtheria toxoid, tetanus toxoid, and three purified pertussis antigens [pertussis toxoid (PT), filamentous hemagglutinin (FHA) and pertactin (PRN/69 kiloDalton outer membrane protein)] adsorbed on aluminium salts. It also contains three types of inactivated polio viruses (type 1: Mahoney strain; type 2: MEF-1 strain; type 3: Saukett strain).

The diphtheria and tetanus toxoids obtained from cultures of *Corynebacterium diphtheriae* and *Clostridium tetani* are inactivated and purified. The acellular pertussis vaccine components (PT, FHA and pertactin) are prepared by growing phase I *Bordetella pertussis* from which the PT, FHA and pertactin are extracted and purified. FHA and pertactin are treated with formaldehyde, PT is treated with glutaraldehyde and formaldehyde, and irreversibly inactivated.

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

INFANRIX®-IPV meets the World Health Organisation requirements for the manufacture of biological substances, of diphtheria, tetanus, pertussis and combined vaccines, and of inactivated poliomyelitis vaccines.

A 0.5 ml dose of vaccine contains not less than 25 Lf ( $\approx$  min. 30 IU) of adsorbed diphtheria toxoid, not less than 10 Lf ( $\approx$  min. 40 IU) of adsorbed tetanus toxoid, 25  $\mu$ g of PT, 25  $\mu$ g of FHA, 8  $\mu$ g of pertactin, 40 D antigen units of type 1 (Mahoney), 8 D antigen units of type 2 (MEF-1) and 32 D antigen units of type 3 (Saukett) of the polio virus.

## **PHARMACEUTICAL FORM**

Suspension, Injection.

## **USES**

### **INDICATIONS**

INFANRIX®-IPV is indicated for active primary immunisation against diphtheria, tetanus, pertussis, and poliomyelitis.

INFANRIX®-IPV is also indicated as a booster dose for children who have previously been immunised with DTP and polio antigens.

## **ACTIONS**

*Not applicable*

## **DOSAGE AND ADMINISTRATION**

### **POSODOLOGY**

The primary vaccination schedule consists of three doses in the first year of life. An interval of at least 1 month should be respected between doses.

In order to maintain protection a booster dose is recommended. An interval of at least 6 months after completion of primary vaccination schedule should be adhered to. Local immunisation schedule recommendations should be followed for primary and booster doses.

Data on the use of the vaccine as a booster has been obtained for children up to 13 years of age.

### **METHOD OF ADMINISTRATION**

INFANRIX®-IPV is for deep intramuscular injection. For infants, the preferred site is the anterolateral aspect of the thigh; in older children, vaccine should be administered in the deltoid.

It is preferable that each subsequent dose is given at alternate sites.

INFANRIX®-IPV should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects. Firm pressure should be applied to the injection site (without rubbing) for at least two minutes.

### **CONTRA-INDICATIONS**

INFANRIX®-IPV should not be administered to subjects with known hypersensitivity to any component of the vaccine, or to subjects having shown signs of hypersensitivity after previous administration of diphtheria, tetanus, pertussis, or inactivated poliomyelitis vaccines.

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

### **SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE**

As with other vaccines, the administration of INFANRIX®-IPV should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection, however, is not a contra-indication.

It is good clinical practice that 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 occur in temporal relation to receipt of DTP-containing vaccine, the decision to give subsequent doses of vaccine containing the pertussis component should be carefully considered. There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks, particularly since the events

are not associated with permanent sequelae. According to available clinical data, the risk benefit ratio of acellular pertussis vaccine is better than the risk benefit ratio of whole cell pertussis vaccine. The following events were previously considered contra-indications for DTPw and can now be considered precautions :

- Temperature of  $\geq 40.0$  °C (rectal) within 48 hours, not due to another identifiable cause.
- Collapse or shock-like state (hypotonic-hypo-responsive episode) within 48 hours of vaccination.
- Persistent, inconsolable crying lasting  $\geq 3$  hours, occurring within 48 hours of vaccination.
- Convulsions with or without fever, occurring within 3 days of vaccination.

In children with progressive neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy, it is better to defer pertussis (Pa or Pw) immunization 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.

A history of febrile convulsions, a family history of convulsions, a family history of Sudden Infant Death Syndrome (SIDS) or a family history of an adverse event following DTP and/or IPV vaccination do not constitute contra-indications.

Human Immunodeficiency Virus (HIV) infection is not considered as a contra-indication.

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

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<sup>®</sup>-IPV contains traces of neomycin and polymyxin. The vaccine should be used with caution in patients with known hypersensitivity to one of these antibiotics.

As with all diphtheria, tetanus, and pertussis vaccines, the vaccine should be given deep intramuscularly.

INFANRIX<sup>®</sup>-IPV 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<sup>®</sup>-IPV should under no circumstances be administered intravenously.

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.

### ***INTERACTION WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION***

It is current practice in paediatric vaccination to co-administer different vaccines during the same session, where injectable vaccines should always be given at different injection sites.

Infanrix<sup>®</sup>-IPV can be administered concomitantly with hepatitis B vaccine, and/or Haemophilus influenzae vaccine, the injections being applied at different injection sites. Routine simultaneous administration of Hib vaccine and hepatitis B vaccine may be given to children who are at the recommended age to receive these vaccines.

Although data on the concomitant administration of Infanrix®-IPV and measles, mumps and rubella combined vaccine and varicella vaccine are not available, it is generally accepted that they may be given at the same time if separate injection sites are used.

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.

### **USE DURING PREGNANCY AND LACTATION**

Adequate human data on use during pregnancy or lactation and adequate animal reproduction studies are not available.

### **EFFECTS ON ABILITY TO DRIVE AND USE MACHINES**

Not applicable.

### **ADVERSE EFFECTS**

#### **Clinical trial experience:**

The safety profile presented below is based on data from more than 2200 subjects.

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

Frequencies per dose are defined as follows:

Very common:  $\geq 10\%$

Common:  $\geq 1\%$  and  $< 10\%$

Uncommon:  $\geq 0.1\%$  and  $< 1\%$

Rare:  $\geq 0.01\%$  and  $< 0.1\%$

Very rare:  $< 0.01\%$

Blood and lymphatic system disorders

Rare: Lymphadenopathy<sup>1</sup>

Metabolism and nutrition disorders

Very common: appetite lost

Psychiatric disorders:

Very common: restlessness, crying abnormal, irritability

Nervous system disorders:

Very common: headache<sup>1</sup> (age range 6-13 years old), somnolence

Respiratory, thoracic and mediastinal disorders:

Rare: bronchitis<sup>2</sup>, cough<sup>2</sup>

Gastrointestinal disorders:

Common: nausea<sup>1</sup>, vomiting, diarrhoea

Skin and subcutaneous tissue disorders

Uncommon: dermatitis allergic

Rare: urticaria, rash<sup>2,3</sup>

General disorders and administration site conditions:

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

Common: local swelling at the injection site ( $>50$  mm)<sup>4</sup>, asthenia, malaise<sup>1</sup>, injection site reactions including induration

Uncommon: diffuse swelling of the injected limb, sometimes involving the adjacent joint<sup>4</sup>, fever<sup>5</sup> ( $>39.5^{\circ}\text{C}$ )

***Post-marketing surveillance:***

Blood and lymphatic system disorders

Thrombocytopenia<sup>6</sup>

Immune system disorders

Allergic reactions, including anaphylactic<sup>2</sup> and anaphylactoid reactions

Nervous system disorders:

Collapse or shock-like state (hypotonic-hyporesponsiveness episode), convulsions (with or without fever) within 2 to 3 days of vaccination  
Respiratory disorders:

Apnoea<sup>2</sup>

Skin and subcutaneous tissue disorders

Pruritus, angioneurotic oedema<sup>2</sup>

General disorders and administration site conditions:

Swelling of the entire injected limb<sup>4</sup>, injection site vesicles

<sup>1</sup>reported only with booster vaccination

<sup>2</sup>reported with GSK's DTPa containing vaccines

<sup>3</sup>uncommonly reported with booster vaccination

<sup>4</sup>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 may be more frequent (very common and common, respectively) when the booster dose is administered between 4 and 6 years. These reactions resolve over an average of 4 days.

<sup>5</sup>commonly reported with booster vaccination

<sup>6</sup>reported with D and T vaccines

***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.

***PHARMACOLOGICAL PROPERTIES***

***PHARMACODYNAMIC PROPERTIES***

Immune response to the DT components:

One month after a primary vaccination course more than 99% of infants vaccinated with INFANRIX<sup>®</sup>-IPV had antibody titers of  $\geq 0.1$  IU/ml to both tetanus and diphtheria.

Following administration of a booster dose of INFANRIX<sup>®</sup>-IPV, more than 99.5% of children had antibody titers of  $\geq 0.1$  IU/ml for both antigens.

#### Immune response to the Pa component:

One month after the 3-dose primary vaccination course with INFANRIX<sup>®</sup>-IPV 100% of infants were seropositive for the three pertussis components (PT, FHA, pertactin), and the overall response rates for each of the three individual pertussis antigens were  $\geq 94\%$ .

A booster response was seen in the vast majority of vaccinees against the pertussis antigens; lower response rates were seen in studies where the pre-vaccination levels of antibodies were high. All subjects were seropositive one month after this dose.

#### Protective efficacy of the Pa component:

As the immune response to pertussis antigens following INFANRIX<sup>®</sup>-IPV administration is equivalent to that of Infanrix<sup>®</sup>, it can be assumed that the protective efficacy of the two vaccines will also be equivalent.

The clinical protection of the DTPa component, against WHO-defined typical pertussis ( $\geq 21$  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 (National Institute of Health - USA) sponsored efficacy study performed in Italy (2,4,6 months schedule). The vaccine efficacy was found to be 84%. In a follow-up study of the same cohort, the efficacy was confirmed for up to 4 years of age.

#### Immune response to the IPV component :

One month after the primary vaccination, the overall seropositivity for each of the three serotypes (type 1, 2 and 3) was  $\geq 99.5\%$ .

Following administration of a booster dose of INFANRIX<sup>®</sup>-IPV, 100% of children were seropositive for the three serotypes.

In all booster trials, vaccination induced a marked increase in antibody levels with respect to pre-booster values.

### **PHARMACOKINETIC PROPERTIES**

Evaluation of pharmacokinetic properties is not required for vaccines.

### **PHARMACEUTICAL PARTICULARS**

#### **LIST OF EXCIPIENTS**

Sodium chloride, Aluminum salts, Medium 199 (as stabilizer including amino acids mineral salts and vitamins), water for injections.

## **RESIDUES**

Potassium Chloride  
Disodium phosphate  
Monopotassium phosphate  
Polysorbate 80  
Glycine  
Formaldehyde  
Neomycin sulphate  
Polymyxin B sulphate

## **INCOMPATIBILITIES**

INFANRIX® -IPV should not be mixed with other vaccines in the same syringe.

## **SHELF-LIFE**

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

The shelf life of the vaccine is 36 months.

## **SPECIAL PRECAUTIONS FOR STORAGE**

INFANRIX® -IPV should be stored at +2°C to +8°C.

The vaccine should not be frozen. Discard if it has been frozen.

## **NATURE AND CONTENT OF CONTAINER**

INFANRIX® -IPV is a turbid white suspension presented in a prefilled syringe. Upon storage, a white deposit and clear supernatant can be observed.

The prefilled syringes are made of neutral glass type I, which conforms to European Pharmacopoeia Requirements.

## **INSTRUCTIONS FOR USE/HANDLING**

The vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine.

Since a white sediment may form during storage, INFANRIX® -IPV should be well shaken.

## **MEDICINE CLASSIFICATION**

Prescription Medicine

## **PACKAGE QUANTITIES**

Prefilled syringes in packs of 1 or 10.

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