

DATA SHEET

NAME OF MEDICINAL PRODUCT

BOOSTRIX[®] -IPV

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

PRESENTATION

BOOSTRIX[®]-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).

1 dose (0.5 ml) contains:

Diphtheria toxoid¹ not less than 2 International Units (IU) (2.5 Lf)

Tetanus toxoid¹ not less than 20 International Units (IU) (5 Lf)

Bordetella pertussis antigens

Pertussis toxoid¹ 8 micrograms

Filamentous Haemagglutinin¹ 8 micrograms

Pertactin¹ 2.5 micrograms

Inactivated poliovirus

type 1 (Mahoney strain)² 40 D-antigen unit

type 2 (MEF-1 strain)² 8 D-antigen unit

type 3 (Saukett strain)² 32 D-antigen unit

¹adsorbed on aluminium hydroxide, hydrated (Al(OH)₃) 0.3 milligrams Al³⁺

and aluminium phosphate (AlPO₄) 0.2 milligrams Al³⁺

² propagated in VERO cells

BOOSTRIX[®]-IPV is a turbid white suspension.

The final vaccine also contains aluminium hydroxide and aluminium phosphate as adjuvants, sodium chloride, Medium 199, water for injections, and traces of formaldehyde, polysorbate 80, neomycin sulfate and polymyxin sulfate.

The manufacture of this product includes exposure to bovine derived materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

PHARMACEUTICAL FORM

Suspension, Injection.

USES

INDICATIONS

BOOSTRIX[®]-IPV is indicated for booster vaccination against diphtheria, tetanus, pertussis and poliomyelitis of individuals from the age of seven years onwards (see DOSAGE AND ADMINISTRATION).

BOOSTRIX[®]-IPV is not intended for primary immunisation.

ACTIONS

Not applicable

DOSAGE AND ADMINISTRATION

POSODOLOGY

A single 0.5 ml dose of the vaccine is recommended.

BOOSTRIX[®]-IPV may be administered from the age of seven years onwards. BOOSTRIX[®]-IPV should be administered in accordance with official recommendations and/or local practice regarding the use of vaccines that provide low (adult) dose diphtheria toxoid plus tetanus toxoid in combination with pertussis and poliomyelitis antigens.

BOOSTRIX[®]-IPV can be used in the management of tetanus prone injuries in persons who have previously received a primary vaccination series of tetanus toxoid vaccine. Tetanus immunoglobulin should be administered concomitantly in accordance with official recommendations.

Repeat vaccination against diphtheria, tetanus and poliomyelitis should be performed at intervals as per official recommendations.

METHOD OF ADMINISTRATION

BOOSTRIX[®]-IPV is for deep intramuscular injection preferably in the deltoid region.

CONTRA-INDICATIONS

BOOSTRIX[®]-IPV should not be administered to subjects with known hypersensitivity after previous administration of diphtheria, tetanus, pertussis or poliomyelitis vaccines or to any component of the vaccine (see PHARMACEUTICAL PARTICULARS).

BOOSTRIX[®]-IPV contains traces of neomycin and polymyxin. The vaccine should not be used in subjects with known hypersensitivity to neomycin and polymyxin.

BOOSTRIX[®]-IPV is contra-indicated if the subject 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 and poliomyelitis vaccines.

BOOSTRIX[®]-IPV should not be administered to subjects who have experienced neurological complications following an earlier immunisation against diphtheria and/or tetanus (for convulsions or hypotonic-hyporesponsive episodes, see SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE).

SPECIAL WARNINGS AND SPECIAL 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).

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

If any of the following events are known to have occurred in temporal relation to receipt of pertussis-containing vaccine in infancy, the decision to give doses of pertussis-containing vaccines should be carefully considered:

Temperature of $\geq 40.0^{\circ}\text{C}$ within 48 hours of vaccination, 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 reaction following the administration of the vaccine.

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.

BOOSTRIX[®]-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.

BOOSTRIX[®]-IPV should in no circumstances be administered intravascularly.

A history or a family history of convulsions and a family history of an adverse event following DTP 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.

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 with any vaccine, a protective immune response may not be elicited in all vaccines.

INTERACTION WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION

Concomitant use with other inactivated vaccines and with immunoglobulin is unlikely to result in interference with the immune responses.

When considered necessary, BOOSTRIX®-IPV can be given concomitantly with other vaccines or immunoglobulins.

As with other vaccines, patients receiving immunosuppressive therapy or patients with immunodeficiency may not achieve an adequate response.

USE DURING PREGNANCY AND LACTATION

Human data on the use of BOOSTRIX®-IPV during pregnancy are not available. However, animal studies showed no reproductive toxicity or teratogenic effects. As with other inactivated vaccines, one does not expect vaccination with BOOSTRIX®-IPV to harm the fetus. However, the vaccine should be used during pregnancy only when clearly needed, and the possible advantages outweigh the possible risks for the fetus.

The safety of BOOSTRIX®-IPV when administered to breast-feeding women has not been evaluated.

It is unknown whether BOOSTRIX®-IPV is excreted in human breast milk.

BOOSTRIX®-IPV should only be used during breast-feeding when the possible advantages outweigh the potential risks.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The vaccine is unlikely to produce an effect on the ability to drive and use machines.

ADVERSE EFFECTS

The safety profile presented below is based on data from clinical trials where BOOSTRIX®-IPV was administered to 908 children (from 4 to 9 years of age) and 955 adults, adolescents and children (above 10 years of age).

The most common events occurring after vaccine administration were local injection site reactions (pain, redness and swelling) reported by 31.3 – 82.3% of subjects overall. These had their onset within the first day after vaccination. All resolved without sequelae.

Adverse reactions reported are listed according to the following frequency:

Very common $\geq 1/10$

Common $\geq 1/100$ and $< 1/10$

Uncommon $\geq 1/1000$ and $< 1/100$

Rare $\geq 1/10,000$ and $< 1/1000$

Very rare $< 1/10,000$

Children from 4 to 9 years of age

Blood and lymphatic system disorders

Uncommon: lymphadenopathy

Metabolism and nutrition disorders

Common: anorexia

Psychiatric disorders

Common: irritability

Uncommon: sleep disorder, apathy

Nervous system disorders

Very common: somnolence
Common: headache

Respiratory, thoracic and mediastinal disorders

Uncommon: dry throat

Gastrointestinal disorders

Uncommon: diarrhoea, vomiting, abdominal pain, nausea

General disorders and administration site conditions

Very common: injection site reactions (including pain, redness and swelling)
Common: fever ≥ 37.5 °C (including fever > 39 °C), injection site reactions (such as haemorrhage)
Uncommon: fatigue

Adults, adolescents and children from the age of 10 years onwards

Infections and infestations

Uncommon: oral herpes

Blood and lymphatic system disorders

Uncommon: lymphadenopathy

Metabolism and nutrition disorders

Uncommon: decreased appetite

Nervous system disorders

Very common: headache
Uncommon: paraesthesia, somnolence, dizziness

Respiratory, thoracic and mediastinal disorders

Uncommon: asthma

Gastrointestinal disorders

Common: gastrointestinal disorders

Skin and subcutaneous tissue disorders

Uncommon: pruritus

Musculoskeletal and connective tissue disorders

Uncommon: myalgia, arthralgia

General disorders and administration site conditions

Very common: injection site reactions (including pain, redness and swelling), fatigue
Common: fever ≥ 37.5 °C, injection site reactions (such as haematoma)
Uncommon: fever > 39 °C, chills, pain

The following adverse reactions were additionally reported during clinical trials with GlaxoSmithKline's other reduced-antigen content diphtheria-tetanus-acellular pertussis vaccine (Boostrix) where Boostrix was administered to 839 children (from 4 to 9 years of age) and 1931 adults, adolescents and children (above 10 years of age):

Children from 4 to 9 years of age

Infections and infestations

Uncommon: upper respiratory tract infection

Nervous system disorders

Uncommon: disturbances in attention

Eye disorders

Uncommon: conjunctivitis

Gastrointestinal disorders

Common: gastrointestinal disorders

Skin and subcutaneous tissue disorders

Uncommon: rash

General disorders and administration site conditions

Uncommon: injection site reactions (such as induration), pain

Adults, adolescents and children from the age of 10 years onwards

Infections and infestations

Uncommon: upper respiratory tract infection, pharyngitis

Nervous system disorders

Uncommon: syncope

Respiratory, thoracic and mediastinal disorders

Uncommon: cough

Gastrointestinal disorders

Common: nausea

Uncommon: diarrhoea, vomiting

Skin and subcutaneous tissue disorders

Uncommon: hyperhidrosis, rash

Musculoskeletal and connective tissue disorders

Uncommon: joint stiffness, musculoskeletal stiffness

General disorders and administration site conditions

Very common: malaise

Common: injection site reactions (such as injection site mass and injection site abscess sterile)

Uncommon: influenza like illness

Subjects fully primed with 4 doses of DTPa followed by BOOSTRIX[®]-IPV at around 4-8 years of age show no increased reactogenicity after the second BOOSTRIX[®]-IPV dose administered 5 years later.

Subjects fully primed with 4 doses of DTPw followed by a BOOSTRIX®-IPV around 10 years of age show an increase of local reactogenicity after an additional Boostrix dose administered 10 years later.

Post Marketing Data

The following adverse reactions were reported during post marketing surveillance after vaccination with BOOSTRIX®-IPV:

Immune system disorders

Very rare: allergic reactions, including anaphylactic and anaphylactoid reactions

General disorders and administration site conditions

Rare: injection site induration

The following adverse reactions were additionally reported during post marketing surveillance after vaccination with GlaxoSmithKline's other reduced-antigen content diphtheria-tetanus-acellular pertussis vaccine (Boostrix):

Blood and lymphatic system disorders

Rare: angioedema

Nervous system disorders

Rare: convulsions (with or without fever)

Skin and subcutaneous tissue disorders

Rare: urticaria

General disorders and administration site conditions

Rare: extensive swelling of the vaccinated limb, asthenia

OVERDOSE

Cases of overdose have been reported during post-marketing surveillance. Adverse events following overdosage, when reported, were similar to those reported with normal vaccine administration.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC PROPERTIES

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

One month post vaccination with BOOSTRIX®-IPV, immune responses in 1469 subjects were the following:

Antigen	Response (% vaccinees)	Adults, adolescents and children from the age of 4 years onwards*
Diphtheria	≥ 0.1 IU/ml	83.5 – 100%
Tetanus	≥ 0.1 IU/ml	99.6 – 100%
Pertussis		

Pertussis toxoid	Vaccine response	94.2 – 97.8%
Filamentous haemagglutinin	Vaccine response	90.1 – 97.2%
Pertactin	Vaccine response	96.5 – 99.3%
Inactivated poliomyelitis		
Type 1	Seroprotection \geq 8	99.6 – 100%
Type 2	Seroprotection \geq 8	99.6 – 100%
Type 3	Seroprotection \geq 8	99.1 – 100%

*In clinical studies, seroprotection and vaccine response rates to all antigens after a booster dose of BOOSTRIX[®]-IPV were similar to the licensed controlled vaccines studied.

As with other adult-type Td vaccines, BOOSTRIX[®]-IPV induces higher seroprotection rates and higher titres of both anti-D and anti-T antibodies in children and adolescents as compared to adults.

The pertussis antigens contained in BOOSTRIX[®]-IPV are an integral part of the paediatric acellular pertussis combination vaccine (INFANRIX[®]), for which efficacy after primary vaccination has been demonstrated in the following 3-dose primary studies :

- 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%.

- an 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, efficacy persisted undiminished up to 5 years after completion of primary vaccination without administration of a booster dose against pertussis.

This study assessed duration of protection of *INFANRIX* given in a 3-dose schedule to infants. A similar duration of protection cannot be assumed to apply to older children or adults given a single dose of *BOOSTRIX-IPV*, regardless of previous vaccination against pertussis.

Although the protective efficacy of *BOOSTRIX-IPV* has not been demonstrated in adolescents and adult age groups, vaccinees in these age groups who received *BOOSTRIX-IPV* achieved anti-pertussis antibody titres greater than those in the German household contact study where the protective efficacy of *INFANRIX* was 88.7%.

There are currently no data which demonstrate a reduction of transmission of pertussis after immunisation with *BOOSTRIX-IPV*. However, it could be expected that immunisation of immediate close contacts of newborn infants, such as parents, grandparents healthcare workers and childcare workers would reduce exposure of pertussis to infants not yet adequately protected through immunisation.

Persistence of immunity to diphtheria, tetanus, pertussis and polio

Five years following vaccination with *BOOSTRIX-IPV*, the following seroprotection / seropositivity rates were observed in 344 children from the age of 4 onwards:

Antigen	Seroprotection/seropositivity	Children from the age of 4 years onwards (% vaccinees)
Diphtheria	\geq 0.1 IU/ml	89.4%
	\geq 0.016 IU/ml*	98.2%
Tetanus	\geq 0.1 IU/ml	98.5%

Pertussis Pertussis toxoid Filamentous haemagglutinin Pertactin	≥ 5 EL.U/ml	40.9% 99.7% 97.1%
Poliovirus type 1 Poliovirus type 2 Poliovirus type 3	≥ 8 ED50	98.8% 99.7% 97.1%

*Percentage of subjects with antibody concentrations associated with protection against disease (≥ 0.1 IU/ml by ELISA assay or ≥ 0.016 IU/ml by an in-vitro Vero-cell neutralisation assay).

The following seroprotection / seropositivity rates for diphtheria, tetanus and pertussis were observed 3 to 3.5 years, 5 to 6 years and 10 years following vaccination with Boostrix (dTPa component of *BOOSTRIX-IPV*) in children, adolescents and adults:

Antigen	Seroprotection/ seropositivity	Adults and adolescents from the age of 10 years onwards (% vaccinees)					
		3-3.5 years persistence		5 years persistence		10 years persistence	
		Adult	Adole- scent	Adult	Adole- scent	Adult	Adole- scent
Diphtheria	≥ 0.1 IU/ml*	71.2%	91.6%	84.1%	86.8%	64.6%	82.4%
	≥ 0.016 IU/ml*	97.4%	100%	94.4%	99.2%	89.9%	98.6%
Tetanus	≥ 0.1 IU/ml	94.8%	100%	96.2%	100%	95.0%	97.3%
Pertussis Pertussis toxoid Filamentous haemagglutinin Pertactin	≥ 5 EL.U/ml	90.6%	81.6%	89.5%	76.8%	85.6%	61.3%
		100%	100%	100%	100%	99.4%	100%
		94.8%	99.2%	95.0%	98.1%	95.0%	96.0%

* Percentage of subjects with antibody concentrations associated with protection against disease (≥ 0.1 IU/ml by ELISA assay or ≥ 0.016 IU/ml by an in-vitro Vero-cell neutralisation assay).

BOOSTRIX-IPV administered in subjects ≥40 years of age with an incomplete, unknown or no history of a primary series of diphtheria and tetanus toxoid vaccination history induced an antibody response against pertussis and protected against tetanus and diphtheria in the majority of cases.

Two subsequent doses maximised the vaccine response against diphtheria and tetanus when administered at one and six months.

Vaccination with second dose of BOOSTRIX-IPV

The immunogenicity of *BOOSTRIX-IPV*, administered 5 years after a previous booster dose of *BOOSTRIX-IPV* at 4 to 8 years of age, has been evaluated. One month post vaccination, ≥ 99 % of subjects were seropositive against pertussis and seroprotected against diphtheria, tetanus and all three polio types.

The immunogenicity of Boostrix, administered 10 years after a previous booster dose with Boostrix or reduced-antigen content diphtheria, tetanus and acellular pertussis vaccines has been evaluated in adults. One month after the decennial Boostrix dose, ≥99 % of subjects were seroprotected against diphtheria and tetanus and all were seropositive for antibodies against pertussis antigens PT, FHA and PRN.

PHARMACOKINETIC PROPERTIES

Evaluation of pharmacokinetic properties is not required for vaccines.

PHARMACEUTICAL PARTICULARS

LIST OF EXCIPIENTS

Medium 199 (as stabilizer containing amino acids, mineral salts, vitamins and other substances)

Sodium chloride

Water for injections.

INCOMPATIBILITIES

BOOSTRIX[®] -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 3 years.

SPECIAL PRECAUTIONS FOR STORAGE

BOOSTRIX[®] -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

BOOSTRIX[®] -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

Prior to vaccination, the vaccine should be well shaken in order to obtain a homogeneous turbid white suspension and visually inspected for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine.

Upon removal from refrigerator, the vaccine is stable for 8 hours at + 21°C.

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

MEDICINE CLASSIFICATION

Prescription Medicine

PACKAGE QUANTITIES

Prefilled syringes in packs of 1 or 10.

Syringes come with or without needles.

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DATE OF PREPARATION

25 February 2011

Version: 3.0

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