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**BOOSTRIX® PRODUCT INFORMATION**

Combined diphtheria-tetanus-acellular pertussis (dTpa) vaccine

**DESCRIPTION**

BOOSTRIX dTpa vaccine is a sterile suspension which contains diphtheria toxoid, tetanus toxoid and three purified antigens of *Bordetella pertussis* [pertussis toxoid (PT), pertussis filamentous haemagglutinin (FHA) and pertactin (PRN)] adsorbed onto aluminium salts.

The diphtheria and tetanus toxins are obtained from cultures of *Corynebacterium diphtheriae* and *Clostridium tetani* and are then detoxified and purified. The acellular pertussis vaccine components (PT, FHA and PRN) are extracted from phase I *Bordetella pertussis*, and are then purified and stabilised.

A 0.5 ml dose of vaccine contains not less than 2 IU (2.5 Lf U) of diphtheria toxoid, not less than 20 IU (5Lf U) of tetanus toxoid, 8 µg of PT, 8 µg of FHA and 2.5 µg of PRN. The diphtheria toxoid, tetanus toxoid and acellular pertussis vaccine (dTpa) components are adsorbed on 0.5mg aluminium in the form of aluminium hydroxide and aluminium phosphate, and suspended in isotonic sodium chloride. The vaccine preparation also contains phenoxyethanol as a preservative.

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.

BOOSTRIX meets the World Health Organisation requirements for biological substances and for diphtheria and tetanus vaccines. No substances of human origin are used in its manufacture.

**CLINICAL PHARMACOLOGY**

BOOSTRIX (dTpa vaccine) induces antibodies against all vaccine components.

## Clinical Trials

Immune response results to the diphtheria, tetanus and acellular pertussis components in the comparative studies (dTpa versus dT) of booster vaccination in different age groups are presented in the table below.

Age at booster	Previous Vaccinations	Results following vaccination with dTpa (N)				
		anti-PT*	anti-FHA*	anti-PRN*	anti-diphtheria †	anti-tetanus†
10-13 years	4 doses DTPw (primary plus booster)	92.1% (441)	96.8% (447)	98.9% (447)	100% (447)	100% (447)
11-17 years	4 doses DTPw (primary plus booster)	100% (40)	95.0% (40)	100% (40)	100% (40)	100% (40)
≥ 18 years**	Variable vaccination histories	95.0% (522)	99.2% (520)	98.5% (522)	92.7% (519)	99.8% (523)

† Percentage of vaccinees having anti-diphtheria and anti-tetanus antibody titres  $\geq 0.1$  IU/ml post-vaccination

\* Percentage of vaccinees having anti-PT, anti-FHA, anti-PRN antibody titres  $\geq$  cut-off (ie, 5 EU/ml) post-vaccination for initially seronegative subjects; or the percentage of vaccinees having a 2-fold increase in anti-PT, anti-FHA, anti-PRN antibody titres post-vaccination for initially seropositive subjects

\*\* Pooled results from two pivotal studies in adults

N= number of subjects.

Results of the comparative studies with commercial dT vaccines indicates that the degree and duration of protection would not be different from those obtained with these vaccines.

The GMT values for the three pertussis antigens following a booster dose of BOOSTRIX to adolescents and adults are provided in the following tables:

Antigen	10-13 years of age (N for post-booster*)	GMT (EI.U/mL) pre-booster	GMT (EI.U/mL) post-booster#
<b>PT</b>	441	9.7	117.6
<b>FHA</b>	447	58.3	923.3
<b>PRN</b>	447	17.5	594.8

# One month after vaccination

\* the number of subjects included in the pre-booster analysis differs

Antigen	≥ 19 years of age (N for post-booster*)	GMT (EI.U/mL) pre-booster	GMT (EI.U/mL) post-booster#
<b>PT</b>	427	8.8	88.1
<b>FHA</b>	426	40.6	1178.9
<b>PRN</b>	427	11.0	472.8

# One month after vaccination

\* the number of subjects included in the pre-booster analysis differs

## **Protective efficacy of pertussis**

There is currently no correlate of protection defined for pertussis; however, the protective efficacy of GlaxoSmithKline Biologicals' DTPa (INFANRIX®) vaccine against WHO-defined typical pertussis ( $\geq 21$  days of paroxysmal cough with laboratory confirmation) was 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%. Protection against laboratory confirmed mild disease, defined as 14 days or more of cough of any type was 73% and 67% when defined as 7 days or more of cough of any type.

- an NIH sponsored efficacy study performed in Italy (2, 4, 6 months schedule).

The vaccine efficacy was found to be 84%. When the definition of pertussis was expanded to include clinically milder cases with respect to type and duration of cough, the efficacy of INFANRIX® was calculated to be 71% against  $>7$  days of any cough and 73% against  $>14$  days of any cough. In a follow-up of the same cohort, the efficacy was confirmed up to 5 years after completion of primary vaccination without administration of a booster dose of pertussis.

The 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, regardless of previous vaccination against pertussis.

Although the protective efficacy of BOOSTRIX has not been demonstrated in adolescents and adult age groups, vaccinees in these age groups who received BOOSTRIX 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. However, it could be expected that immunisation of immediate close contacts of newborn infants, such as parents, grandparents and healthcare workers, would reduce exposure of pertussis to infants not yet adequately protected through immunisation.

## **INDICATIONS**

BOOSTRIX is indicated for booster vaccination against diphtheria, tetanus and pertussis of individuals aged ten years and older.

## **CONTRAINDICATIONS**

BOOSTRIX 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 or pertussis vaccines.

As with other vaccines, the administration of BOOSTRIX should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection, however, is not a contraindication.

BOOSTRIX 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, adult-type combined diphtheria–tetanus vaccine should be used.

BOOSTRIX should not be administered to subjects who have experienced transient thrombocytopenia or neurological complications following an earlier immunisation against diphtheria and/or tetanus.

## **PRECAUTIONS**

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

It is good clinical practice that immunisation should be preceded by a review of the medical history (especially with regard to previous immunisation and possible occurrence of undesirable events) and a clinical examination.

If any of the following events have occurred in temporal relation to receipt of pertussis containing vaccines, the decision to give doses of pertussis containing vaccines, should be carefully considered.

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.

- 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-hyporesponsive 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) 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 anaphylactic reactions following the administration of the vaccine.

A history or a family history of convulsions and a family history of an adverse event following DTP vaccination do not constitute contra-indications.

HIV infection is not considered a contraindication for diphtheria, tetanus and pertussis (whole-cell or acellular) immunisation. However in patients with immunodeficiency or in patients receiving immunosuppressive therapy, an adequate immunologic response may not be achieved. In these patients, when tetanus vaccine is needed for tetanus prone wound, plain tetanus vaccine should be used.

The duration of immunity afforded by pertussis components of the vaccine has not been established.

## **INTERACTIONS**

Concomitant administration of other vaccines with BOOSTRIX has not been studied.

Different injectable vaccines should always be administered at different injection sites.

**BOOSTRIX must not be mixed with other vaccines.**

### **Use In Pregnancy (Category B2)**

Adequate human data on use during pregnancy and adequate animal reproduction studies are not available. Therefore, BOOSTRIX should be used during pregnancy only when clearly needed, and the possible advantages outweigh the possible risks for the foetus. When protection against tetanus is sought, consideration should be given to tetanus or combined diphtheria-tetanus vaccines. As with all inactivated vaccines, one does not expect harm to the foetus.

### **Use In Lactation**

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

### **Effects on the ability to drive and use machines**

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

## **ADVERSE REACTIONS**

### **Clinical Trial Experience**

During controlled clinical studies, diary cards were used to monitor signs and symptoms in all vaccinees following administration of a dose of BOOSTRIX. The following table summarises data from two pivotal studies for solicited local and general symptoms reported during a 15 day follow-up period after vaccination. Onset of the majority of local and general symptoms occurred within 48 hours of vaccination. All symptoms resolved without sequelae. A causal relationship between these events and vaccination has not necessarily been established.

<b>Solicited Symptoms</b>	<b>Incidence %</b>					
	BOOSTRIX administered to Adolescent subjects aged 10-17 years	Adolescent comparator group who received separate Td and aP (ap) vaccines		BOOSTRIX administered to Adult subjects aged ≥18 years	Adult comparator group who received separate Td and aP (ap) vaccines	
	<i>BOOSTRIX</i>	<i>Td</i>	<i>aP</i>	<i>BOOSTRIX</i>	<i>Td*</i>	<i>aP*</i>
<i>Local reactions</i>	<i>N=448</i>	<i>n=60</i>	<i>n=59</i>	<i>N=438</i>	<i>n=54</i>	<i>n=55</i>
Pain	79.0	83.3	67.8	72.6	85.2	56.4
Redness (≥ 5cm)	5.8	16.7	0	2.5	7.4	0
Swelling (≥ 5cm)	7.8	10.0	1.7	2.5	5.6	0
<i>General symptoms</i>						
Fever (≥ 37.5°C)	8.9	8.3	5.1	18.5	33.3	12.7
Fever (≥ 39.1°C)	0.4	0	0	0.2	0	0
Malaise	27.7	26.7	20.3	19.2	20.4	14.5
Fatigue	56.2	50.0	40.7	27.2	25.9	23.6
Vomiting	4.0	5.0	3.4	3.4	3.7	5.5
Headache	51.3	51.7	35.6	37.0	44.4	47.3
Dizziness	20.5	26.7	13.6	10.0	3.7	9.1

\* This data is from the first vaccination of either of these comparator vaccines

### **Other events**

Other unsolicited events reported in clinical trials for BOOSTRIX are listed below. It should be noted however that causality has not necessarily been established for these events.

The events are listed within body systems and categorised by frequency according to the following definitions: common events reported at a frequency of less than 1/10 but greater

or equal to 1/100 patients; uncommon events reported at a frequency of less than 1/100 but greater or equal to 1/1,000 patients; rare events reported at a frequency of less than 1/1,000 patients.

**Application site:** *Common:* injection site reaction

**Dermatological:** *Uncommon:* pruritis

**Body as a whole:** *Common:* pain, irritability, loss of appetite; *Uncommon:* sweating

**Musculoskeletal:** *Uncommon:* myalgia, arthrosis, hypertonia

**Lymphatic system:** *Uncommon:* lymphadenopathy

**Gastrointestinal:** *Common:* diarrhoea

### **Post-marketing experience**

Post-marketing experience with BOOSTRIX is currently limited.

Extremely rare cases of collapse or shock-like state (hypotonic-hyporesponsiveness episode) and convulsions within 2 to 3 days of vaccination have been reported following DTPa and DTPa combination vaccines. All the subjects recovered totally and spontaneously without sequelae. At the present time, there have been no collapse or shock-like episodes reported following administration of BOOSTRIX.

Very rare allergic reactions, including anaphylactoid reactions, have also been reported following administration of DTPa containing vaccines.

### **DOSAGE AND ADMINISTRATION**

All parenteral drug and vaccine products should be inspected visually for any particulate matter or discolouration prior to administration. Before use of BOOSTRIX, the vaccine should be well shaken to obtain a homogenous turbid suspension. Discard the vaccine if it appears otherwise.

#### **Dosage**

Each dose consists of a 0.5mL ready to use sterile suspension.

#### **Administration**

BOOSTRIX is administered by deep intramuscular injection. THE VACCINE SHOULD NEVER BE ADMINISTERED INTRAVENOUSLY.

BOOSTRIX 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.

This product is for use by one patient on a single occasion. Discard remaining contents.

### **Immunisation Schedule**

BOOSTRIX can be given in accordance with the current local medical practices for booster vaccination with adult-type combined diphtheria-tetanus vaccine, when a booster against pertussis is desired.

The NHMRC previously recommended boosting against diphtheria and tetanus every 10 years in adults. The recommendation has changed such that the NHMRC now recommends boosting against diphtheria and tetanus at 15-19 years and again at 50 years. The NHMRC currently have no recommendation regarding the timing and frequency of booster doses against pertussis in adults.

Individuals with an incomplete, or no, history of a primary series of diphtheria and tetanus toxoids should not be vaccinated with BOOSTRIX. BOOSTRIX is not precluded in subjects with an incomplete, or no, history of previous pertussis vaccination. However, a booster response will only be elicited in individuals who have been previously primed by vaccination or by natural infection.

*Tetanus-prone injury*:- In case of tetanus-prone injury, BOOSTRIX can be used as an alternative to adult-type combined diphtheria-tetanus in individuals with no history of tetanus toxoid within the preceding five years, if a booster against diphtheria and pertussis is additionally desired.

### **STORAGE**

BOOSTRIX should be stored at +2°C and +8°C. DO NOT FREEZE, discard if vaccine has been frozen. The expiry date of the vaccine is indicated on the label and packaging.

### **PRESENTATIONS**

BOOSTRIX is presented as a turbid white suspension in a glass vial or glass prefilled syringe. Upon storage a white deposit and clear supernatant can be observed.

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

**MANUFACTURER:**

GlaxoSmithKline Biologicals SA  
rue de l'Institut 89  
1330 Rixensart, Belgium.

**DISTRIBUTED IN AUSTRALIA BY:**

GlaxoSmithKline Australia Pty Ltd  
1061 Mountain Highway  
Boronia 3155 VIC

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