AUSTRALIAN PRODUCT INFORMATION

BOOSTRIX (combined diphtheria, tetanus, acellular pertussis (dTpa)) suspension for injection

1 NAME OF THE MEDICINE

Combined diphtheria-tetanus-acellular pertussis (dTpa) vaccine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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.

1 dose (0.5 mL) contains:

Diphtheria toxoid[1]	not less than 2 International Units (IU) (2.5 Lf)
Tetanus toxoid[1]	not less than 20 International Units (IU) (5 Lf)

Bordetella pertussis antigens

Pertussis toxoid[1]	8 micrograms
Filamentous Haemagglutinin[1]	8 micrograms
Pertactin[1]	2.5 micrograms

[1] adsorbed on aluminium hydroxide hydrate (Al(OH)3)	0.3 milligrams Al3+
and aluminium phosphate (AlPO4)	0.2 milligrams Al3+

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.

No substances of human origin are used in its manufacture.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

This medicine contains less than 1 mmol (39 mg) per dose of potassium and less than 1 mmol (23 mg) per dose of sodium, i.e., essentially ‘potassium-free’ and ‘sodium-free’.

3 PHARMACEUTICAL FORM

BOOSTRIX is a turbid white suspension for injection.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

BOOSTRIX is indicated for booster vaccination against diphtheria, tetanus and pertussis of individuals aged four years and older (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION).

BOOSTRIX is also indicated for passive protection against pertussis in early infancy following maternal immunisation during pregnancy (see Section 4.2 DOSE AND METHOD OF ADMINISTRATION, Section 4.6 FERTILITY, PREGNANCY AND LACTATION and 5.1 PHARMACODYNAMIC PROPERTIES).

The use of BOOSTRIX should be in accordance with official recommendations.

4.2 DOSE AND METHOD OF 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. Do not administer the vaccine if it appears otherwise.

Dosage

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

BOOSTRIX can be administered to pregnant women during the second or the third trimester of pregnancy in accordance with official recommendations (see Section 4.1 THERAPEUTIC INDICATIONS, Section 4.6 FERTILITY, PREGNANCY AND LACTATION and 5.1 PHARMACODYNAMIC PROPERTIES).

Administration

BOOSTRIX is administered by deep intramuscular injection, preferably in the deltoid region. 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. If in accordance with official recommendations, the vaccine may need to be administered subcutaneously to these subjects. With both routes of administration, 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.

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

BOOSTRIX can be given in accordance with current local recommendations for booster vaccination with reduced-content combined diphtheria-tetanus vaccine, when a booster against pertussis is desired.

BOOSTRIX may also be administered to adolescents with unknown vaccination status or incomplete vaccination against diphtheria, tetanus and pertussis. BOOSTRIX is not precluded in adult subjects with an incomplete, or no, history of previous pertussis vaccination. However, a booster response will only be elicited in adults who have been previously primed by vaccination or by natural infection (see Section 5.1 PHARMACODYNAMIC PROPERTIES).

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.

BOOSTRIX can be used as an alternative to diphtheria-tetanus in the management of tetanus prone injuries in persons who have previously received a primary vaccination series of tetanus toxoid vaccine. If required, tetanus immunoglobulin may be administered concomitantly in accordance with official recommendations.

4.3 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 contraindicated 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 and tetanus vaccines.

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

diphtheria and/or tetanus (for convulsions or hypotonic-hyporesponsive episodes, see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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 ≥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.

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.

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. If in accordance with official recommendations, the vaccine may need to be administered subcutaneously to these subjects. With both routes of administration, firm pressure should be applied to the injection site (without rubbing) for at least two minutes.

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

Human Immunodeficiency Virus (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.

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 vaccinees.

Use in the elderly

No data available.

Paediatric use

See Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

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

If BOOSTRIX is to be given at the same time as another injectable vaccine or immunoglobulin, the products should always be administered at different sites.

BOOSTRIX must not be mixed with other vaccines.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No human data are available. In combined fertility and embryofetal development studies in rats and rabbits, female fertility was unaffected by IM administration of BOOSTRIX twice before mating with 2/5x (rats) or 1x (rabbits) the human dose.

Use in pregnancy

(Pregnancy Category A)

BOOSTRIX can be used during the second or third trimester of pregnancy in accordance with official recommendations

For data relating to the prevention of pertussis disease in infants born to women vaccinated during pregnancy, see Section 5.1 PHARMACODYNAMIC PROPERTIES.

Safety data from a randomised controlled clinical trial (341 pregnancy outcomes) and from a prospective observational study (793 pregnancy outcomes) where BOOSTRIX was administered to pregnant women during the third trimester have shown no vaccine related adverse effect on pregnancy or on the health of the foetus/newborn child.

Safety data from prospective clinical studies on the use of BOOSTRIX or BOOSTRIX-IPV during the first and second trimester of pregnancy are not available.

Data from post-marketing surveillance where pregnant women were exposed to BOOSTRIX or to BOOSTRIX-IPV (dTpa-inactivated poliovirus vaccine) in the second or third trimester do not suggest any elevated frequency or unusual patterns of adverse events in pregnant women and their newborn child following pertussis vaccination.

As with other inactivated vaccines, it is not expected that vaccination with BOOSTRIX harms the foetus at any trimester of pregnancy.

Although lower concentrations of antibodies against some pertussis antigens were observed post primary and post booster vaccination in infants and toddlers born to mothers vaccinated with BOOSTRIX during pregnancy, clinical data demonstrated such immune interferences to be non-clinically relevant. The lower antibody concentrations did not prevent effective priming of the immune system of infants born to BOOSTRIX-vaccinated mothers as indicated by the establishment of a strong booster response against all vaccine antigens by the age of 11-18 months.

Combined embryo-foetal development studies in which rats or rabbits were IM administered BOOSTRIX twice before mating and several times during gestation (and once during lactation in rats) with 2/5x (rats) or 1x (rabbits) the human dose showed no effects on embryo-foetal development, nor on postnatal development in rats.

When protection against tetanus is sought, consideration should be given to tetanus or combined diphtheria-tetanus vaccines.

Use in lactation

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

It is unknown whether BOOSTRIX is excreted in human breast milk.

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

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Clinical Trial Experience

The safety profile below is based on data from clinical trials 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).

The adverse reactions are listed within body systems and are listed according to the following frequency:

- Very common: ≥1/10
- Common: ≥1/100 and <1/10
- Uncommon: ≥1/1000 and <1/100
- Rare: ≥1/10,000 and <1/1000
- Very rare: <1/10,000

Children from 4 to 9 years of age

Infections and infestations

Uncommon: upper respiratory tract infection

Metabolism and nutrition disorders

Common: anorexia

Psychiatric disorders

Very common: irritability

Nervous system disorders

Very common: somnolence

Common: headache

Uncommon: disturbances in attention

Eye disorders

Uncommon: conjunctivitis

Gastrointestinal disorders

Common: diarrhoea, vomiting, gastrointestinal disorders

Skin and subcutaneous tissue disorders

Uncommon: rash

General disorders and administration site conditions

Very common: injection site reactions (including pain, redness and swelling), fatigue

Common: fever ≥ 37.5°C (including fever > 39°C),

Uncommon: other 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

Blood and lymphatic system disorders

Uncommon: lymphadenopathy

Nervous system disorders

Very common: headache

Common: dizziness

Uncommon: syncope

Respiratory, thoracic and mediastinal disorders

Uncommon: cough

Gastrointestinal disorders

Common: nausea, gastrointestinal disorders

Uncommon: diarrhoea, vomiting

Skin and subcutaneous tissue disorders

Uncommon: hyperhidrosis, pruritus, rash

Musculoskeletal and connective tissue disorders

Uncommon: arthralgia, myalgia, joint stiffness, musculoskeletal stiffness

General disorders and administration site conditions

Very common: injection site reactions (including pain, redness and swelling), fatigue, malaise

Common: fever ≥ 37.5°C, injection site reactions (such as injection site mass and injection site abscess sterile)

Uncommon: fever > 39°C, influenza like illness, pain

Reactogenicity after a repeat dose of BOOSTRIX

Data on 146 subjects suggests a small increase in local reactogenicity (pain, redness, swelling) with repeated vaccination according to a 0, 1, 6 months schedule in adults (>40 years of age).

Subjects fully primed with 4 doses of DTPw followed by BOOSTRIX dose around 10 years of age show an increase of local reactogenicity after an additional BOOSTRIX dose administered 10 years later compared to after the first BOOSTRIX dose.

Post-marketing experience

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.

Blood and lymphatic system disorders

Rare: angioedema

Immune system disorders

Very rare: allergic reactions, including anaphylactic and anaphylactoid reactions

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

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 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.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

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

Clinical trials

Immune response

Immune response results to the diphtheria, tetanus and acellular pertussis components in four comparative studies (dTpa versus dT) of booster vaccination in different age groups are presented in the Table 1 below.

Table 1: Immune responses to diphtheria, tetanus and acellular pertussis components following booster vaccination in adults and adolescents above 10 years of age

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 ≥ 0.1 IU/ml post-vaccination
* Percentage of vaccinees having anti-PT, anti-FHA, anti-PRN antibody titres ≥ cut-off (i.e., 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 Tables 2 and 3:

Table 2: GMT values for pertussis antigens after vaccination of adolescents between 10 and 13 years of age with BOOSTRIX

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

One month after vaccination
* The number of subjects included in the pre-booster analysis differs

Table 3: GMT values for pertussis antigens after vaccination of adults with BOOSTRIX

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

One month after vaccination
* The number of subjects included in the pre-booster analysis differs

A pooled analysis of the Immune response results to the diphtheria, tetanus and acellular pertussis components from 15 comparative and noncomparative clinical studies are presented in Table 4 (children 4-9 years of age) and Table 5 (adults and adolescents above 10 years of age) below. Approximately one month following booster vaccination with BOOSTRIX, the following seroprotection / seropositivity rates were observed:

Table 4: Pooled analysis of immune responses to diphtheria, tetanus and acellular pertussis components following booster vaccination in children 4-9 years of age (at least 415 subjects)

Antigen	Response[(1)]		% Vaccinees (CI)	GMC (CI)
Diphtheria	≥0.1 IU/mL	Pre	78.8% (74.5-82.6)	0.351 (0.183-0.675)
		Post	99.8% (98.7-100)	5.705 (3.379-9.634)
Tetanus	≥0.1 IU/mL	Pre	88.7% (85.3-91.6)	0.500 (0.282-0.886)
		Post	100% (99.1-100)	14.449 (11.172-18.687)°
Pertussis				
Pertussis toxoid	≥5 EL.U/mL	Pre	31.2% (26.7-35.9)	4.3 (3.3-5.7)
		Post	99.0% (97.6-99.7)	72.3 (62.6-83.5)
Filamentous haemagglutinin	≥5 EL.U/mL	Pre	87.3% (83.7-90.4)	35.6 (16.9-75.2)
		Post	100% (99.1-100)	536.1 (341.3-842.0)
Pertactin	≥5 EL.U/mL	Pre	69.2% (64.5-73.6)	20.7 (5.2-82.7)
		Post	99.8% (98.7-100)	307.7 (82.1-1152.8)

[(1)]Response: Where at the specified time point, a concentration of antibodies against diphtheria and tetanus ≥0.1 IU/mL was considered as seroprotection and a concentration of antibodies against pertussis ≥5 EL.U/mL was considered as seropositivity

% Vaccinees = percentage of subjects with concentration within the specified range
GMC = geometric mean antibody concentration calculated on all subjects
CI = Confidence interval (95%)
Pre = blood sample taken prior to booster vaccination
Post = blood sample taken approximately one month after booster vaccination

Table 5: Pooled analysis of immune responses to diphtheria, tetanus and acellular pertussis components following booster vaccination in adults and adolescents above 10 years of age (at least 1670 subjects)

Antigen	Response[(1)]		% Vaccinees (CI)	GMC (CI)
Diphtheria	≥0.1 IU/mL	Pre	68.4% (66.1-70.6)	0.274 (0.166-0.451)
		Post	97.2% (96.3-97.9)	3.382 (2.184-5.235)
Tetanus	≥0.1 IU/mL	Pre	88.6% (87.0-90.0)	0.654 (0.418-1.024)
		Post	99.0% (98.4-99.4)	8.491 (5.632-12.801)
Pertussis				
Pertussis toxoid	≥5 EL.U/mL	Pre	56.9% (54.5-59.3)	7.3 (5.9-9.0)
		Post	97.8% (96.9-98.4)	85.2 (69.8-104.0)
Filamentous haemagglutinin	≥5 EL.U/mL	Pre	96.9% (96.0-97.7)	35.3 (28.9-43.2)
		Post	99.9% (99.7-100)	830.9 (725.6-951.5)
Pertactin	≥5 EL.U/mL	Pre	70.1% (67.8-72.3)	11.4 (8.7-14.8)
		Post	99.4% (98.9-99.7)	480.0 (342.8-672.1)

[(1)]Response: Where at the specified time point, a concentration of antibodies against diphtheria and tetanus ≥0.1 IU/mL was considered as seroprotection and a concentration of antibodies against pertussis ≥5 EL.U/mL was considered as seropositivity
% Vaccinees = percentage of subjects with concentration within the specified range
GMC = geometric mean antibody concentration calculated on all subjects
CI = Confidence interval (95%)
Pre = blood sample taken prior to booster vaccination
Post = blood sample taken approximately one month after booster vaccination

Efficacy in protecting against 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 (≥ 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, childcare workers, would reduce exposure of pertussis to infants not yet adequately protected through immunisation.

Passive protection against pertussis in infants (below 3 months of age) born to mothers vaccinated during pregnancy

In a randomised, cross-over, placebo-controlled study, higher pertussis antibody concentrations were demonstrated at delivery in the cord blood of babies born to mothers vaccinated with BOOSTRIX (N=291) versus placebo (N=292) during the third trimester of pregnancy. The concentrations of antibodies against the pertussis antigens PT, FHA and PRN were respectively 8, 16 and 21 times higher in the cord blood of babies born to vaccinated mothers versus controls. These antibody titres may provide passive protection against pertussis, as shown by observational effectiveness studies.

Immunogenicity in infants and toddlers born to mothers vaccinated during pregnancy

In follow-up trials in more than 500 infants and toddlers born to vaccinated mothers, clinical data 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.

Effectiveness in the protection against pertussis disease in infants born to women vaccinated during pregnancy

BOOSTRIX or BOOSTRIX-IPV vaccine effectiveness (VE) was evaluated in three observational studies, in UK, Spain and Australia. The vaccine was used during the third trimester of pregnancy to protect infants below 3 months of age against pertussis disease, as part of a maternal immunisation programme.

Details of each study design and results are provided in Table 6 below:

Table 6: VE against pertussis disease for infants below 3 months of age born to mothers vaccinated during the third trimester of pregnancy with BOOSTRIX/BOOSTRIX-IPV

Study Location	**Vaccine**	**Study design**	**Vaccination Effectiveness**
UK	BOOSTRIX-IPV	Retrospective, screening method	88% (95% CI: 79, 93)
Spain	BOOSTRIX	Prospective, matched case-control	90.9% (95% CI: 56.6, 98.1)
Australia	BOOSTRIX	Prospective, matched case-control	69% (95% CI: 13, 89)

CI: confidence interval

If maternal vaccination occurs within two weeks before delivery, VE in the infant may be lower than the figures in the table.

Persistence of the immune response

The following responses for diphtheria, tetanus and pertussis were observed 3 to 3.5 years and 5 years following vaccination with BOOSTRIX in children (Table 7):

Table 7: Data on persistence up to 3-3.5 years (study APV-124) and 5-6 years (Tdap0.3-004) after vaccination of children between 4 to 6 years of age with BOOSTRIX in study APV-118 (ATP[1])

Antigen	**Response[2]**	**Children from 4 to 6 years of age (% vaccinees) (CI)**	
		3-3.5 years persistence	**5-6 years persistence**
Diphtheria	≥ 0.1 IU/mL[3]	97.5 % (93.0-99.5)	94.2 % (85.8-98.4)
	≥ 0.016 IU/mL[3]	100 % (97.0-100)	Not determined
Tetanus	≥ 0.1 IU/mL	98.4 % (94.2-99.8)	98.5 % (92.1-100)
Pertussis			
Pertussis toxoid	≥ 5 EL.U/mL	58.7 % (49.4-67.6)	51.5 % (39.0-63.8)
Filamentous haemagglutinin	≥ 5 EL.U/mL	100 % (96.9-100)	100 % (94.8-100)
Pertactin	≥ 5 EL.U/mL	99.2 % (95.5-100)	100 % (94.9-100)

(1) ATP: According to protocol – includes all eligible participants, who had received a single booster dose of BOOSTRIX, for whom immunogenicity data was available for at least one antigen at the specified time-point.
(2) Response: Where, at the specified time point, a concentration of antibodies against diphtheria and tetanus ≥ 0.1 IU/mL was considered as seroprotection and a concentration of antibodies against pertussis ≥ 5 EL.U/mL was considered as seropositivity
(3) Percentage of participants 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).
CI = Confidence Interval (95%)

The following responses for diphtheria, tetanus and pertussis were observed 3 to 3.5 years, 5 years and 10 years following vaccination with BOOSTRIX in adolescents (Table 8) and adults (Table 9):

Table 8: Data on persistence up to 3-3.5 years (study dTpa-017), 5 years (study dTpa-030) and 10 years (study dTpa-040) after vaccination of adolescents between 10 and 13 years of age with BOOSTRIX in study dTpa-004 (ATP[1])

Antigen	Response[2]	Adolescents[3] % Vaccines (CI)		
		3-3.5 years persistence	5 years persistence	10 years persistence
Diphtheria	≥ 0.1 IU/mL[4]	91.6% (87.6 – 94.7)	86.8% (82.0-90.7)	82.4% (71.8-90.3)
	≥ 0.016 IU/mL[4]	100% (98.2-100)	99.2% (96.9-99.9)	98.6% (92.7-100)
Tetanus	≥ 0.1 IU/mL	100% (98.6-100)	100% (98.6-100)	97.3% (90.6-99.7)
Pertussis				
Pertussis toxoid	≥ 5 EL.U/mL	81.6% (76.4-86.1)	76.8% (71.1-81.9)	61.3% (49.4-72.4)
Filamentous haemagglutinin	≥ 5 EL.U/mL	100% (98.6-100)	100% (98.6-100)	100% (95.2-100)
Pertactin	≥ 5 EL.U/mL	99.2% (97.3-99.9)	98.1% (95.5-99.4)	96.0% (88.8-99.2)

(1) ATP: According to protocol – includes all eligible participants, who had received a single booster dose of BOOSTRIX, for whom immunogenicity data was available for at least one antigen at the specified time-point.
(2) Response: Where, at the specified time point, a concentration of antibodies against diphtheria and tetanus ≥ 0.1 IU/mL was considered as seroprotection and a concentration of antibodies against pertussis ≥ 5 EL.U/mL was considered as seropositivity
(3) The term 'adolescents' reflects the age at which the participants received their first vaccination with BOOSTRIX
(4) Percentage of participants 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).
CI = Confidence Interval (95%)

Table 9: Data on persistence up to 3-3.5 years (study dTpa-021), 5 years (study dTpa-027) and 10 years (study dTpa-039) after vaccination of adults between 19 and 70 years of age with BOOSTRIX in study dTpa-002 (ATP[1])

Antigen	Response[2]	Adults[3] % Vaccines (CI)		
		3-3.5 years persistence	5 years persistence	10 years persistence
Diphtheria	≥ 0.1 IU/mL[4]	71.2% (65.8-76.2)	84.1% (78.7-88.5)	64.6% (56.6-72.0)
	≥ 0.016 IU/mL[4]	97.4% (95.6-99.2)	94.4% (90.6-97.0)	89.9% (84.1-94.1)
Tetanus	≥ 0.1 IU/mL	94.8% (91.8-97.0)	96.2% (93.0-98.3)	95.0% (90.4-97.8)
Pertussis				
Pertussis toxoid	≥ 5 EL.U/mL	90.6% (86.8-93.6)	89.5% (84.9-93.1)	85.6% (79.2-90.7)
Filamentous haemagglutinin	≥ 5 EL.U/mL	100% (98.8-100)	100% (98.5-100)	99.4% (96.6-100)
Pertactin	≥ 5 EL.U/mL	94.8% (91.7-97.0)	95.0% (91.4-97.4)	95.0% (90.3-97.8)

(1) ATP: According to protocol – includes all eligible participants, who had received a single booster dose of BOOSTRIX, for whom immunogenicity data was available for at least one antigen at the specified time-point.
(2) Response: Where, at the specified time point, a concentration of antibodies against diphtheria and tetanus ≥ 0.1 IU/mL was considered as seroprotection and a concentration of antibodies against pertussis ≥ 5 EL.U/mL was considered as seropositivity
(3) The term 'adults' reflects the age at which the participants received their first vaccination with BOOSTRIX
(4) Percentage of participants 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).
CI = Confidence Interval (95%)

Immune response in subjects with unknown/incomplete/no primary vaccination history

Adolescents: After administration of one dose of BOOSTRIX to 83 adolescents aged from 11 to 18 years, without previous pertussis vaccination and no vaccination against diphtheria and tetanus in the previous 5 years, all subjects were seroprotected against tetanus and diphtheria. The seropositivity rate after one dose varied between 87% and 100% for the different pertussis antigens.

Adults: After administration of one dose of BOOSTRIX to 139 adults ≥40 years of age that had not received any diphtheria and tetanus containing vaccine in the past 20 years, more than 98.5% of adults were seropositive for all three pertussis antigens and 81.5% and 93.4%

were seroprotected against diphtheria and tetanus respectively. After administration of two additional doses one and six months after the first dose, the seropositivity rate was 100% for all three pertussis antigens and the seroprotection rates for diphtheria and tetanus reached 99.3% and 100% respectively. While the study included patients who had either not received vaccination against pertussis or had received pertussis vaccination more than 40 years before, almost all subjects were positive for anti-FHA and anti-PT antibodies and approximately half were positive to anti-PRN antibodies at baseline.

Immune response after a repeat dose of BOOSTRIX

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.

5.2 PHARMACOKINETIC PROPERTIES

Not relevant to vaccines.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

BOOSTRIX has not been evaluated for genotoxicity.

Carcinogenicity

BOOSTRIX has not been evaluated for carcinogenicity.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

The diphtheria toxoid, tetanus toxoid and acellular pertussis vaccine (dTpa) components are adsorbed on 0.5 mg aluminium and suspended in isotonic sodium chloride.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

BOOSTRIX should be stored in a refrigerator (2°C - 8°C). DO NOT FREEZE. Discard if vaccine has been frozen.

Stability data indicate that the vaccine is stable at temperatures up to 37°C for 7 days. **At the end of this period, Boostrix must be used or discarded. It must not be returned to storage.** These data are intended to guide healthcare professionals in case of temporary temperature excursion only.

Protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

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

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

Not all pack sizes and presentations may be distributed in Australia.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Not relevant to vaccines.

CAS number

Not relevant to vaccines.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription Only Medicine

8 SPONSOR

GlaxoSmithKline Australia Pty Ltd
Level 4, 436 Johnston Street,
Abbotsford, Victoria, 3067

9 DATE OF FIRST APPROVAL

20 April 2009

10 DATE OF REVISION

24 August 2022

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
2	Added statement on potassium-free and sodium-free content
6.1	Removal of reference to excipients formaldehyde, polysorbate 80 and glycine
6.4	Inclusion of time out of refrigeration statement
6.5	Removal of reference to vial presentation

Version 12.0