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BOOSTRIX®-IPV
PRODUCT INFORMATION

NAME OF THE MEDICINE

BOOSTRIX-IPV is a combined diphtheria, tetanus, acellular pertussis (dTpa) and inactivated poliovirus vaccine.

DESCRIPTION

BOOSTRIX-IPV is a sterile suspension for injection which contains diphtheria toxoid (D), tetanus toxoid (T), three purified antigens of *Bordetella pertussis* [pertussis toxoid (PT), pertussis filamentous haemagglutinin (FHA) and pertactin (PRN)] and 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 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
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
[1]adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$)	0.3 milligrams Al^{3+}
and aluminium phosphate ($AlPO_4$)	0.2 milligrams Al^{3+}
[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.

PHARMACOLOGY

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

Clinical trials

More than 1500 vaccinees have received a dose of BOOSTRIX-IPV in clinical studies conducted in children (4 to 8 years of age), adolescents (10 to 14 years of age) and adults (>14 years of age). The children were previously primed with 4 doses of DTPa and at least 3 doses of OPV or IPV, the adolescents with DTPw and the recommended local schedule for polio, and the adults had a variable immunisation history but all had received a primary course of diphtheria and tetanus vaccination. One month post vaccination with BOOSTRIX-IPV, immune responses in 1469 subjects were the following:

Immune response to the D and T components:

100% of children and adolescents (<18 years) had antibody titres of ≥ 0.1 IU/mL for both antigens. 86.8 % of subjects ≥ 18 years achieved antibody levels against D of ≥ 0.016 IU/mL (by ELISA ± Vero-cell testing), and 99.6% achieved antibody levels against T of ≥ 0.1 IU/mL (by ELISA). For both diphtheria and tetanus, serum antibody levels ≥ 0.01 IU/mL are considered protective.

Immune response to the Pa component:

A total of 97.5% of subjects were seropositive for antibodies to all Pa components (PT, FHA or PRN) (ELISA, cut-off 5 EL.U/mL). The vaccine response rates (> two-fold rise in antibody titres, or ≥ the cut-off in initially seronegative subjects) after BOOSTRIX-IPV were >94% for PT and PRN, and >90% for FHA.

Protective efficacy of the Pa component:

There is currently no serological correlate of protection defined for pertussis; however, the protective efficacy of GSK's 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%.

- 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.

Immune response to the IPV component:

More than 99% of subjects had antibody titres ≥ 8 for all three polio serotypes one month after a booster dose of BOOSTRIX-IPV.

Antibody titres ≥ 8 are deemed to correlate with protection against polio.

Table 1: Study dTpa-IPV-001 – a partially blinded, randomised, phase III clinical trial to assess the immunogenicity of BOOSTRIX-IPV (dTpa-IPV) one month after vaccination of healthy children 4 to 8 years of age: Geometric Mean Concentrations (GMCs) pre- and post-vaccination.

Antigen	**Booster immunisation GMC** (95% confidence interval)	
	Pre-booster	**Post-booster***
Diphtheria Toxoid (N=778 [pre] and 779 [post])	0.19 (0.18 – 0.21)	4.46 (4.16 – 4.79)
Tetanus Toxoid (N=778 [pre] and 779 [post])	0.33 (0.30 – 0.36)	13.89 (13.11 – 14.72)
Pertussis Toxoid (N=777 [pre] and 775 [post])	4.4 (4.1 – 4.6)	52.0 (48.9 – 55.2)
Pertussis FHA (N=776 [pre] and 779 [post])	61.5 (56.0 – 67.5)	535.8 (509.3 – 563.7)

Pertussis PRN (N=779)	30.5 (27.8 – 33.5)	477.0 (446.9 – 509.2)
Poliovirus Type 1 (N=748 [pre] and 749 [post])	103.8 (94.8 – 113.7)	3514 (3292 – 3751)
Poliovirus Type 2 (N=749 [pre] and 733 [post])	141.7 (131.0 – 153.3)	3388 (3190 – 3598)
Poliovirus Type 3 (N=734 [pre] and 715 [post])	47.3 (42.1 – 53.1)	3772 (3528 – 4033)

**One month after vaccination*
Note: Primary immunisation with four doses of DTPa vaccine
The figures relating to poliovirus types 1,2 and 3 are geometric mean titres.
N = Number of subjects
Assay cut-offs for each antigen are as follows: D & T: ≥0.1 IU/mL; PT, FHA & PRN: 5 EL.U/mL; POLIO types 1,2,3: ≥8.

Table 2: Study dTpa-IPV-002 – an open, randomised, multicenter phase II clinical trial to assess the immunogenicity of BOOSTRIX-IPV (dTpa-IPV) one month after vaccination of healthy adolescents 10 to 14 years of age: Geometric Mean Concentrations (GMCs) pre- and post- vaccination.

Antigen	**Booster immunisation GMC** (95% confidence interval)	
	Pre-booster	**Post-booster***
Diphtheria Toxoid (N=429 [pre] and 428 [post])	0.22 (0.20 – 0.25)	2.72 (2.51 – 2.95)
Tetanus Toxoid (N=428)	0.60 (0.55 – 0.67)	13.36 (12.46 – 14.32)
Pertussis Toxoid (N=424)	6.7 (6.0 – 7.5)	96.9 (89.0 – 105.5)
Pertussis FHA (N=429 [pre] and 428 [post])	57.3 (51.5 - 63.7)	743.8 (699.5 – 791.0)
Pertussis PRN (N=429 [pre] and 428 [post])	13.7 (12.2 – 15.4)	356.2 (319.8 – 396.7)
Poliovirus Type 1 (N=128 [pre] and 426 [post])	59.4 (47.6 – 73.9)	4200 (3883 – 4543)
Poliovirus Type 2 (N=127 [pre] and 424 [post])	63.3 (51.4 – 78.0)	2863 (2642 – 3103)
Poliovirus Type 3 (N=126 [pre] and 404 [post])	15.6 (13.1 – 18.6)	4114 (3795 – 4459)

*One month after vaccination
Note: Primary immunisation with DTPw vaccine
The figures relating to poliovirus types 1,2 and 3 are geometric mean titres.
N = Number of subjects
Assay cut-offs for each antigen are as follows: D & T: ≥0.1 IU/mL; PT, FHA & PRN: 5 EL.U/mL; POLIO types 1,2,3: ≥8.

Table 3: Study dTpa-IPV-003 – an open, randomised, multicenter phase III clinical trial to assess the immunogenicity of BOOSTRIX-IPV (dTpa-IPV) one month after vaccination of healthy adolescents ≥ 15 years of age and adults: Geometric Mean Concentrations (GMCs) pre- and post- vaccination

Antigen	Booster immunisation Age ≤ 40 years GMC (95% confidence interval)		Booster immunisation Age >40 years GMC (95% confidence interval)	
	Pre-booster	Post-booster*	Pre-booster	Post-booster*
Diphtheria Toxoid	0.37 (0.29 – 0.47) N = 135	2.01 (1.61 – 2.50) N = 135	0.09 (0.08 – 0.11) N = 126	0.37 (0.28 – 0.49) N = 126
Tetanus Toxoid	1.35 (1.07 – 1.69) N = 135	7.54 (6.66 – 8.54) N = 135	0.78 (0.58 – 1.04) N = 126	5.25 (4.36 – 6.31) N = 126
Pertussis Toxoid	7.4 (6.1 – 8.9) N = 135	84.3 (70.5 – 100.7) N = 132	6.4 (5.4 – 7.7) N = 126	56.8 (48.5 – 66.5) N = 125
Pertussis FHA	42.0 (35.0 – 50.3) N = 134	610.0 (528.9 – 703.6) N = 135	57.3 (49.7 – 66.0) N = 126	594.0 (526.0 – 670.8) N = 125
Pertussis PRN	10.8 (8.6 – 13.6) N = 135	447.2 (344.3 – 580.8) N = 135	7.1 (5.8 – 8.6) N = 126	203.7 (144.8 – 286.7) N = 126
Poliovirus Type 1	89.6 (51.6 – 155.7) N = 32	2445.4 (2024.6 – 2953.6) N = 129	121.4 (73.2 – 201.4) N = 33	1957.3 (1536.6 – 2493.2) N = 122
Poliovirus Type 2	86.5 (59.7 – 125.2) N = 37	1568.8 (1242.3 – 1981.0) N = 126	49.6 (30.8 – 79.9) N = 38	1411.4 (1067.1 – 1866.8) N = 121
Poliovirus Type 3	41.3 (24.1 – 70.7) N = 35	2674.9 (2142.4 – 3339.8) N = 122	55.4 (33.7 – 91.3) N = 36	2244.7 (1748.6 – 2881.7) N = 113

*One month after vaccination

Note: Heterogeneous primary immunisation history: subjects ≤40 years are likely to have received primary vaccination against pertussis with DTPw, subjects >40 years are unlikely to have received primary vaccination against pertussis and would have been more likely to *have been primed through natural infection.*

The figures relating to poliovirus types 1,2 and 3 are geometric mean titres.

N = Number of subjects

Assay cut-offs for each antigen are as follows: D & T: ≥0.1 IU/mL; PT, FHA & PRN: 5 EL.U/mL; POLIO types 1,2,3: ≥8.

Tetanus antibody response in the first 10 days following vaccination

Anti-tetanus toxoid antibodies were measured 10 days after vaccination in a subset of subjects aged 18 years and over in a study in Germany.

Seroprotective antibody concentrations (≥ 0.1 IU/mL) were observed in 95.1% of the subjects having received BOOSTRIX-IPV, 96.5% of the subjects having separate injections of BOOSTRIX and IPV and 92.1% of subjects having received a licensed Td-IPV vaccine. There

thus did not appear to be any significant difference between BOOSTRIX-IPV and the two control groups.

BOOSTRIX-IPV - persistence of immunity to diphtheria, tetanus, pertussis and polio
A total of 344 children vaccinated with BOOSTRIX-IPV between 4 and 8 years of age, had antibody persistence five years later as shown in table 4 below.

Table 4: Study dTpa-IPV-008- antibody persistence data five years after vaccination of children between **4** and 8 years of age in study dTpa-IPV-001 (ATP[1])

Antigen	Response[2]	Number of participants n (N)	Children 9 to 13 years % vaccinees (CI)
Diphtheria	≥ 0.1 IU/mL	305 (341)	89.4% (85.7-92.5)
	≥ 0.016 IU/mL[3]		98.2% (96.3-99.2)
Tetanus	≥ 0.1 IU/mL	337 (342)	98.5% (96.6-99.5)
Pertussis			
Pertussis toxoid	≥ 5 EL.U/mL	138 (337)	40.9% (35.7-46.4)
Filamentous haemagglutinin	≥ 5 EL.U/mL	339 (340)	99.7% (98.4-100)
Pertactin	≥ 5 EL.U/mL	332 (342)	97.1% (94.7-98.6)
Poliovirus			
Poliovirus type 1	≥ 8 ED50	336 (340)	98.8% (97.0-99.7)
Poliovirus type 2	≥ 8 ED50	340 (341)	99.7% (98.4-100)
Poliovirus type 3	≥ 8 ED50	331 (341)	97.1% (94.7-98.6)

(1) ATP: According to protocol – includes all eligible participants, who had received a single booster dose of BOOSTRIX IPV, for whom immunogenicity data was available for at least one antigen at the specified time-point.
(2) Response: Where, after five years, a concentration of antibodies against diphtheria and tetanus ≥ 0.1 IU/mL was considered as seroprotection, a concentration of antibodies against pertussis ≥ 5 EL.U/mL was considered as seropositivity and dilution titres against poliovirus types 1, 2 and 3 of 1:8 were considered as positive.
(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).
n = number of participants with concentration within the specified range
N = number of participants with available results
CI = Confidence Interval (95%)

BOOSTRIX-IPV – vaccination with a second dose

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 participants were seropositive against pertussis and seroprotected against diphtheria, tetanus and all three polio types.

BOOSTRIX (dTpa component of BOOSTRIX-IPV) - persistence of immunity to diphtheria, tetanus and pertussis

The following responses for diphtheria, tetanus and pertussis were observed 3 to 3.5 years, 5 years and 10 years following vaccination with BOOSTRIX (dTpa component of BOOSTRIX-IPV) in adolescents (Table 5) and adults (Table 6):

Table 5: 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 6: 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 adolescents 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%)

BOOSTRIX (dTpa component of BOOSTRIX-IPV) – vaccination with a second dose

The immunogenicity of BOOSTRIX (dTpa component of BOOSTRIX Polio), administered 10 years after a first booster dose with BOOSTRIX or reduced-antigen content diphtheria, tetanus and acellular pertussis vaccines has been evaluated in adolescents and adults. One month post vaccination, >99 % of participants were seroprotected against diphtheria and tetanus and all were seropositive against pertussis.

INDICATIONS

BOOSTRIX-IPV is indicated for booster vaccination against diphtheria, tetanus, pertussis and polio of individuals from the age of four years onwards.

The NHMRC currently recommends only 4 doses of polio vaccines in childhood, and that polio boosters for adults are not necessary unless they are at special risk, such as:

- travellers to areas or countries where poliomyelitis is epidemic or endemic;
- health care workers in possible contact with poliomyelitis cases.

For those exposed to continuing risk of infection a single booster dose is desirable every 10 years.

The NHMRC currently recommends boosting against diphtheria, tetanus and pertussis using an adolescent/adult formulation dTpa at 15 to 17 years of age. Before the eighth birthday,

DTP-containing vaccines should be given, as they contain a larger dose of diphtheria toxoid. After the eighth birthday, smaller doses of toxoid (adult/adolescent formulation dTpa or dT-containing vaccines) should be given.

A booster dose of dTpa is also recommended:

- before planning pregnancy, or for both parents as soon as possible after delivery of an infant
- For adults working with young children
- For any adult expressing an interest in receiving a booster dose of dTpa, provided that a primary course of DTP vaccine has been given in the past.

Clinical data has demonstrated that in adults with an unknown history of pertussis vaccination, the majority had an immunogenic response to pertussis when given BOOSTRIX-IPV (see PHARMACOLOGY).

Finally, all adults who reach the age of 50 years without having received a boosting dose of dT in the previous 5 years should receive a further boosting dose of dT, where the adult/adolescent formulation dTpa can be used instead.

BOOSTRIX-IPV is not intended for primary immunisation.

CONTRAINDICATIONS

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

BOOSTRIX-IPV is contraindicated if the child has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with a pertussis containing vaccine. In these circumstances pertussis vaccination should be discontinued and the vaccination should be continued with diphtheria-tetanus and polio 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 PRECAUTIONS).

PRECAUTIONS

BOOSTRIX-IPV should under no circumstances be administered intravascularly.

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.

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.

If any of the following events are known to have occurred in temporal relation to receipt of pertussis-containing vaccines, the decision to give further 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 of vaccination outweigh the 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.

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 DTPa and/or IPV vaccination do not constitute contra-indications.

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

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 contains traces of neomycin sulfate and polymyxin sulfate. The vaccine should be used with caution in patients with known hypersensitivity to either of these antibiotics.

Human Immunodeficiency Virus (HIV) infection is not considered a contra-indication to BOOSTRIX-IPV vaccination. However in patients with immunodeficiency or in patients receiving immunosuppressive therapy, the expected immunologic response may not be achieved. No data currently exist on use of BOOSTRIX-IPV in these 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.

Effects on Fertility

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

Use During Pregnancy: (Category B1)

Combined embryo fetal development studies in which rats or rabbits were IM administered BOOSTRIX-IPV 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 embryofetal development in either species, nor on postnatal development in rats. Similarly, no effects on embryofetal development were observed in rats IM administered INFANRIX-IPV once prior to gestation and BOOSTRIX-IPV (1/5x the human dose) 4 times during gestation.

As with other inactivated vaccines, it is not expected that vaccination with BOOSTRIX IPV harms the fetus.

However, adequate human data on use of BOOSTRIX-IPV during pregnancy are not available. Therefore, BOOSTRIX IPV should be used during pregnancy only when clearly needed, and the possible advantages outweigh the possible risks for the fetus. When protection against tetanus is sought, consideration should be given to tetanus or combined diphtheria-tetanus vaccines.

Use During Lactation:

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.

Animal reproduction studies in rats have shown that offspring of dams boosted with 1/5 the human dose (based on volume) of BOOSTRIX-IPV during pregnancy have higher serum titres on lactation day 25 than lactation day 4, suggesting maternal transfer of antibodies by milk during lactation.

Genotoxicity
BOOSTRIX-IPV has not been evaluated for genotoxicity.

Carcinogenicity
BOOSTRIX has not been evaluated for carcinogenicity

INTERACTIONS WITH OTHER MEDICINES

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

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

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

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

ADVERSE EFFECTS

Clinical Trial Experience:
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 in both groups were local injection site reactions (pain, redness and swelling). These had their onset within the first day after vaccination. All resolved without sequelae.
The adverse events 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

Blood and lymphatic system disorders

Uncommon: lymphadenopathy

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

Metabolism and nutrition disorders

Common: anorexia

Nervous system disorders

Very common: somnolence
Common: headache

Psychiatric disorders

Common: irritability
Uncommon: sleep disorder, apathy

Respiratory, thoracic and mediastinal disorders

Uncommon: dry throat

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

Blood and lymphatic system disorders

Uncommon: lymphadenopathy

Gastrointestinal disorders

Common: gastrointestinal disorders (nausea, vomiting, diarrhoea and/or abdominal pain)

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

Infections and infestations

Uncommon: oral herpes

Metabolism and nutrition disorders

Uncommon: decreased appetite

Musculoskeletal and connective tissue disorders

Uncommon: myalgia, arthralgia

Nervous system disorders

Very common: headache
Uncommon: paraesthesia, somnolence, dizziness

Respiratory, thoracic and mediastinal disorders

Uncommon: asthma

Skin and subcutaneous tissue disorders

Uncommon: pruritus

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

Eye disorders

Uncommon: conjunctivitis

Gastrointestinal disorders

Common: gastrointestinal disorders (nausea, vomiting, diarrhoea and/or abdominal pain)

General disorders and administration site conditions

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

Infections and infestations

Uncommon: upper respiratory tract infection

Nervous system disorders

Uncommon: disturbances in attention

Skin and subcutaneous tissue disorders

Uncommon: rash

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

Gastrointestinal disorders

Common: nausea
Uncommon: diarrhoea, vomiting

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

Infections and infestations

Uncommon: upper respiratory tract infection, pharyngitis

Musculoskeletal and connective tissue disorders

Uncommon: joint stiffness, musculoskeletal stiffness

Nervous system disorders

Uncommon: syncope

Respiratory, thoracic and mediastinal disorders

Uncommon: cough

Skin and subcutaneous tissue disorders

Uncommon: hyperhidrosis, rash

Collapse or shock-like state (hypotonic-hyporesponsive episode) and convulsions have been reported *very rarely* following immunisation of children with products containing one or more of the antigenic constituents of BOOSTRIX-IPV.

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 surveillance

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, injection site induration

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-IPV, the vaccine should be well shaken to obtain a homogenous turbid suspension. Discard the vaccine if it appears otherwise. The vaccine should be administered immediately after opening.

Dosage

A single 0.5mL dose may be administered from the age of four years onwards.

Administration

BOOSTRIX-IPV is administered by deep intramuscular injection preferably in the deltoid region of the arm. BOOSTRIX-IPV is for use in one patient on one occasion only. Contains no antimicrobial preservative. Any unused product or waste material should be disposed of in accordance with local requirements.

BOOSTRIX-IPV VACCINE SHOULD NEVER BE ADMINISTERED INTRAVENOUSLY.

Individuals with an incomplete, or no, history of a primary series of diphtheria and tetanus toxoids should not be vaccinated with BOOSTRIX-IPV. BOOSTRIX-IPV is not precluded in subjects with an incomplete, or no, history of previous pertussis or polio 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-IPV 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, pertussis and polio is desired in addition to tetanus.

BOOSTRIX-IPV can be used as an alternative to adult type 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.

OVERDOSAGE

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.

STORAGE AND PRESENTATIONS

Storage

BOOSTRIX-IPV should be stored between +2°C and +8°C. DO NOT FREEZE. Discard if vaccine has been frozen. Protect from light.

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

Presentations

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

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

NAME AND ADDRESS OF THE SPONSOR

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POISON SCHEDULE OF THE MEDICINE

Schedule 4– Prescription Only Medicine

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG): 8 July 2004

DATE OF MOST RECENT AMENDMENT: 13 May 2016

Version 6.0