PRODUCT MONOGRAPH

BOOSTRIX®-POLIO

(Combined diphtheria, tetanus, acellular pertussis (adsorbed) and inactivated poliomyelitis) vaccine

Active immunizing agent against infection by diphtheria, tetanus, whooping cough and poliomyelitis

GlaxoSmithKline Inc.
7333 Mississauga Road
Mississauga, Ontario
L5N 6L4

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Combined diphtheria, tetanus, acellular pertussis (adsorbed) and inactivated poliomyelitis vaccine

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Intramuscular	Suspension for injection/ not less than 2.5 limit of flocculation ('Lf'), or 2 IU ('International Units') of diphtheria toxoid; not less than 5 Lf (20 IU) of tetanus toxoid; 8 µg of pertussis toxoid, 8 µg of filamentous haemagglutinin, 2.5 µg of pertactin (69 kDa outer membrane protein); 40 D-antigen units (DU) of Type 1 poliovirus, 8 DU Type 2 polio virus and 32 DU Type 3 polio virus.	Aluminum adjuvant (as aluminum salts), sodium chloride, water for injection and medium 199. Formaldehyde, neomycin and polymyxin are present as traces.

DESCRIPTION

BOOSTRIX®-POLIO (combined diphtheria, tetanus, acellular pertussis (adsorbed) and inactivated poliomyelitis) vaccine is presented as a turbid white suspension in a single dose vial or prefilled syringe. Upon storage, a white deposit and clear supernatant can be observed. This is a normal finding.

INDICATIONS AND CLINICAL USE

BOOSTRIX®-POLIO (combined diphtheria, tetanus, acellular pertussis (adsorbed) and inactivated poliomyelitis) vaccine is indicated for:

- Booster vaccination against diphtheria, tetanus, pertussis and poliomyelitis of individuals from the age of four years onwards.

BOOSTRIX®-POLIO is not intended for primary immunization.

CONTRAINDICATIONS

- Patients who are hypersensitive to any component of the vaccine or to subjects having shown signs of hypersensitivity after previous administration of diphtheria, tetanus, pertussis or poliomyelitis vaccines. For a complete listing, see the DOSAGE FORMS, COMPOSITION and PACKAGING section of the product monograph.
- BOOSTRIX®-POLIO (combined diphtheria, tetanus, acellular pertussis (adsorbed) and inactivated poliomyelitis) vaccine contains traces of neomycin and polymyxin. The vaccine should not be used in subjects with known hypersensitivity to neomycin and polymyxin.
- BOOSTRIX®-POLIO is contraindicated if the subject has experienced an encephalopathy of unknown etiology, occurring within 7 days following previous vaccination with pertussis containing vaccine. In these circumstances, adult-type combined diphtheria tetanus and poliomyelitis vaccine should be used.
- BOOSTRIX®-POLIO should not be administered to subjects who have experienced transient thrombocytopenia or neurological complications following an earlier immunization against diphtheria and/or tetanus.

WARNINGS AND PRECAUTIONS

General

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

As with any other vaccine, BOOSTRIX®-POLIO (combined diphtheria, tetanus, acellular pertussis (adsorbed) and inactivated poliomyelitis) vaccine may not protect 100% of individuals receiving the vaccine.

BOOSTRIX®-POLIO should under no circumstances be administered intravascularly.

As with other vaccines, the administration of BOOSTRIX®-POLIO should be postponed in subjects suffering from moderate or severe illness with or without fever. The presence of minor illnesses with or without a low-grade fever are not a contraindication.

If any of the following events occur in temporal relation to administration of whole-cell DTP or acellular DTP vaccine, the decision to give subsequent doses of vaccine containing the pertussis component should be carefully considered. There may be circumstances, such as high incidence of pertussis, in which the potential benefits outweigh possible risks, particularly since these events have not been proven to cause 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.

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®-POLIO.

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.

Neurologic

In children with progressive neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy, it is better to defer pertussis (Pa or Pw) immunization until the condition is corrected or stable. However, the decision to give pertussis vaccine must be made on an individual basis after careful consideration of the risks and benefits.

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

Hematologic

BOOSTRIX®-POLIO 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 2 minutes.

Immune

HIV infection is not considered as a contraindication. The expected immunological response may not be obtained after vaccination of immunosuppressed patients, e.g. patients on immunosuppressive therapy.

Sensitivity

As with other injectable vaccines, appropriate medication (e.g. Epinephrine 1:1000) should be readily available for immediate use in case of anaphylaxis or anaphylactoid reactions following administration of the vaccine. For this reason, the vaccinee should remain under medical supervision for 30 minutes after immunization. For initial management of anaphylaxis, please refer to the current Canadian Immunization Guide.

Special Populations

Pregnant Women:

Animal studies do not indicate direct or indirect harmful effects with respect to female fertility, pregnancy, embryonal/fetal development, parturition or post-natal development (see TOXICOLOGY).

Although data from post-marketing surveillance where pregnant women were exposed to BOOSTRIX®-POLIO do not suggest vaccine related adverse effect on pregnancy or on the health of the fetus/newborn child, these findings should be interpreted with caution given the limitations associated with the data obtained from post-marketing surveillance.

As with other inactivated vaccines, it is not expected that the antigens contained in BOOSTRIX®-POLIO would harm the fetus. However, BOOSTRIX®-POLIO should only be used during pregnancy when clearly needed and the possible advantages outweigh the possible risks for the fetus.

Limited data indicate that maternal antibodies may reduce the magnitude of the immune response to some vaccines in infants born from mothers vaccinated with BOOSTRIX®-POLIO during pregnancy. The clinical relevance of this observation is unknown.

Nursing Women:

Adequate human data on the use during lactation and adequate animal reproductive studies are not available. BOOSTRIX®-POLIO should be used during lactation, after evaluation of the risk of disease and probable benefit of vaccination.

ADVERSE REACTIONS

Clinical Trial Adverse Drug Reactions

> *Because clinical trials are conducted under very specific conditions the adverse reaction rates events and for approximating rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates*.

The safety profile presented below is based on data from clinical trials where BOOSTRIX®-POLIO 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 pain, redness and swelling reported by 31.3 – 82.3% of subjects overall. These usually had their onset within the first day after vaccination. All resolved without sequelae.

Children from 4 to 9 years of age

Frequency	Adverse Event	System/Organ Class
Very Common: ≥ 1/10	injection site reactions (including pain, redness and swelling)	General disorders and administration site conditions
	somnolence	Nervous system disorders
Common: ≥ 1/100 and <1/10	fever ≥37.5°C (including fever >39°C), injection site reactions (such as haemorrhage)	General disorders and administration site conditions
	anorexia	Metabolism and nutrition disorders
	irritability	Psychiatric disorders
	headache	Nervous system disorders
	gastrointestinal disorders*	Gastrointestinal disorders*
Uncommon: ≥ 1/1000 and <1/100	injection site reactions (such as induration)*, pain*	General disorders and administration site conditions
	fatigue	
	sleep disorder, apathy	Psychiatric disorders
	dry throat	Respiratory, thoracic and mediastinal disorders
	diarrhea, vomiting, abdominal pain, nausea	Gastrointestinal disorders
	upper respiratory tract infection*	Infections and infestations*
	disturbances in attention*	Nervous system disorders*
	conjunctivitis*	Eye disorders*
	rash*	Skin and subcutaneous tissue disorders*

*Refers to adverse reactions additionally reported during clinical trials with BOOSTRIX®, where BOOSTRIX® was administered to 839 children (from 4 to 9 years of age).

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

Frequency	Adverse Event	System/Organ Class
Very Common: ≥ 1/10	injection site reactions (including pain, redness and swelling), fatigue	General disorders and administration site conditions
	malaise*	
	headache	Nervous system disorders
Common: ≥ 1/100 and <1/10	injection site reactions (such as injection site mass and injection site abscess sterile)*	General disorders and administration site conditions
	fever ≥37.5°C, injection site reactions (such as haematoma)	
	gastrointestinal disorders	Gastrointestinal disorders
	nausea*	
Uncommon: ≥ 1/1000 and <1/100	fever > 39°C, chills, pain	General disorders and administration site conditions
	influenza like illness*	
	oral herpes	Infections and infestations
	upper respiratory tract infection*, pharyngitis*	
	lymphadenopathy	Blood and lymphatic system disorders
	decreased appetite	Metabolism and nutrition disorders
	paraesthesia, somnolence, dizziness	Nervous system disorders
	syncope*	
	asthma	Respiratory, thoracic and mediastinal disorders
	cough*	
	pruritus	Skin and subcutaneous tissue disorders
	hyperhidrosis*, rash*	
	myalgia, arthralgia	Musculoskeletal and connective tissue disorders
	joint stiffness*, musculoskeletal stiffness*	
	diarrhea*, vomiting*	Gastrointestinal disorders

*Refers to adverse reactions additionally reported during clinical trials with BOOSTRIX®, where BOOSTRIX® was administered to 1931 adults, adolescents and children (above 10 years of age).

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

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

Post-Market Adverse Drug Reactions

Frequency	Adverse Event	System/Organ Class
Rare: ≥ 1/10,000 and <1/1000	extensive swelling of the vaccinated limb, asthenia	General disorders and administration site conditions
	angioedema	Blood and lymphatic system disorders
	convulsions (with or without fever)	Nervous system disorders
	urticaria	Skin and subcutaneous tissue disorders
Very rare: <1/10,000	allergic reactions, including anaphylactic and anaphylactoid reactions	Immune system disorders

DRUG INTERACTIONS

Drug-Drug Interactions

Concomitant use with other inactivated vaccines or with immunoglobulin has not been studied. There is no evidence, to date, to indicate that co-administration will result in interference with the immune responses. However extrapolation to new future vaccines cannot be made. When considered necessary, BOOSTRIX®-POLIO (combined diphtheria, tetanus, acellular pertussis (adsorbed) and inactivated poliomyelitis) vaccine, can be administered simultaneously with other vaccines or immunoglobulin, at a different injection site.

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

Drug-Lifestyle Interactions

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

DOSAGE AND ADMINISTRATION

Recommended Dose

A single 0.5 mL dose of the vaccine is recommended.

BOOSTRIX®-POLIO (combined diphtheria, tetanus, acellular pertussis and inactivated poliomyelitis) vaccine may be administered from the age of four years onwards.

See official recommendations as per the Canadian Immunization Guide that provide low (adult) dose diphtheria toxoid plus tetanus toxoid in combination with pertussis and poliomyelitis antigens.

There are no data on the duration of protection against pertussis following vaccination with BOOSTRIX®-POLIO.

Repeat vaccination against diphtheria, tetanus and poliomyelitis should be performed at intervals as per official recommendations (generally 10 years).

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

BOOSTRIX®-POLIO is for deep intramuscular injection.

Tetanus Prophylaxis in Wound Management
The following table summarizes the recommended use of immunizing agents in wound management. It is important to ascertain the number of doses of toxoid previously given and the interval since the last dose. When a tetanus booster dose is required, the combined preparation of tetanus and diphtheria toxoid formulated for adults (Td) is preferred. Appropriate cleansing and debridement of wounds is imperative, and use of antibiotics may be considered.

Some individuals with humoral immune deficiency, including those with HIV infection, may not respond adequately to tetanus toxoid. Therefore, tetanus immune globulin (TIG) should be used in addition to tetanus toxoid if a wound occurs that is not clean, regardless of the time elapsed since the last booster.

Table 1 Guide to Tetanus Prophylaxis in Wound Management

History of Tetanus Immunization	Clean, minor wounds		All other wounds	
	Td or Tdap*	Tig**	Td or Tdap*	Tig
Uncertain of < 3 doses of an immunization series†	Yes	No	Yes	Yes
≥ 3 doses received in an immunization series†	No‡	No	No§	No¶

*Adult type combined tetanus and diphtheria toxoids or a combined preparation of diphtheria, tetanus and acellular pertussis. If the patient is < 7 years old, a tetanus toxoid-containing vaccine is given as part of the routine childhood immunization.
**Tetanus immune globulin, given at a separate site from Td (or Tdap).
†The immunization series for tetanus is described in the text (Schedule and Dosage).
‡Yes, if > 10 years since last booster.
§Yes, if > 5 years since last booster. More frequent boosters not required and can be associated with increased adverse events. The bivalent toxoid, Td, is not considered to be significantly more reactogenic than T alone and is recommended for use in this circumstance. The patient should be informed that Td (or Tdap) has been given.
¶Yes, if individuals are known to have a significant humoral immune deficiency state (e.g., HIV, agammaglobulinemia) since immune response to tetanus toxoid may be suboptimal.

Administration
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.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Diphtheria

Diphtheria is a serious communicable disease, primarily a localized and generalized intoxication caused by diphtheria toxin, an extracellular protein metabolite of toxigenic strains of *Corynebacterium diphtheriae*. The disease occurs most frequently in unimmunised or partially immunized individuals. The incidence of diphtheria in Canada has decreased from 9,000 cases reported in 1924 to extremely low levels. Only one or two cases have been reported annually in recent years. The case fatality rate remains 5% to 10%, with the highest death rates in the very young and elderly. If immunization levels are allowed to fall and adults do not receive booster doses, disease re-emergence may appear as demonstrated in the Commonwealth of Independent States (former Soviet Union), where tens of thousands of cases with substantial mortality have been reported. Protection against disease is due to the development of neutralizing antibodies to the diphtheria toxin. Following adequate immunization with diphtheria toxoid, it is generally accepted that protection persists for at least 10 years. Serum antitoxin levels of at least 0.01 antitoxin units per mL are generally regarded as protective. This significantly reduces both the risk of developing diphtheria and the severity of clinical illness. Immunization with diphtheria toxoid does not, however, eliminate carriage of *C. diphtheriae* in the pharynx or nose or on the skin.

Tetanus

Tetanus is an intoxication manifested primarily by neuromuscular dysfunction caused by a potent exotoxin released by *Clostridium tetani*. Immunization is highly effective, provides long lasting protection and is recommended for the entire population. Only 1 to 7 with an average of 5 cases of tetanus are reported annually in Canada while no deaths have been recorded since 1995. The disease continues to occur almost exclusively among persons who are unvaccinated or inadequately vaccinated or whole vaccination histories are unknown or uncertain.

Spores of *C. tetani* are ubiquitous. Naturally acquired immunity to tetanus toxin does not occur. Thus, universal primary immunization and timed booster doses to maintain adequate tetanus antitoxin levels are necessary to protect all age groups. Protection against disease is due to the development of neutralizing antibodies to the tetanus toxin. Tetanus toxoid is a highly effective antigen and a completed primary series generally induces serum antitoxin levels of at least 0.01 antitoxin units per mL, a level which has been reported to be protective. It is generally accepted that protection persists for at least 10 years. To maintain immunity to tetanus following completion of primary immunization, booster doses administered as Td are recommended at 10 yearly intervals.

Pertussis

Pertussis (whooping cough) is a disease of the respiratory tract caused by *Bordetella pertussis*. Pertussis is highly communicable (attack rates in unimmunised household contacts of up to 90% have been reported) and can affect individuals of any age; however, severity is greatest among young infants. Precise epidemiologic data do not exist, since bacteriological confirmation of pertussis can be obtained in less than half of the suspected cases. Most reported illness from *B. pertussis* occurs in infants and young children in whom complications can be severe. Older children, adolescents and adults, in whom classic signs of pertussis infection are often absent, may go undiagnosed, and may serve as reservoirs of disease and may act as the primary source of transmission of the bacillus to infants.

Pertussis epidemics are cyclic, occur every 3 to 4 years and outbreaks continue to occur due to the decline in immunity in individuals who received the whole cell vaccine during childhood; a decline in the population that may have acquired natural infection with longer lasting immunity; improvements in diagnosis and surveillance; and possible genetic changes in current strains compared with the strains of *B. pertussis* from which the original whole cell vaccine was prepared. With the licensure of acellular pertussis vaccines, which have better safety and efficacy profiles, the use of whole cell pertussis vaccines is no longer recommended in Canada.

During the 1980s, pertussis incidence was low, but has increased since 1990 in spite of high vaccine coverage. Over the past 10 years, the annual number of reported cases of pertussis in Canada has ranged from 2,400 to 10,000 although these figures likely under represent the true incidence because of incomplete reporting.

Active surveillance for pertussis has found that 1% to 25% of patients with prolonged cough had *B. pertussis* infection. Using a combination of laboratory methods, the Sentinel Health Unit Surveillance System has documented pertussis infection in 9% to 20% of non improving cough illness of 7 days or more in adolescents and adults.

Canadian studies have estimated that the secondary attack rate of pertussis in adolescents and adults by household contact ranged between 12% and 14% in contacts aged 12 to 17 years, 11% to 18% for those 18 to 29 years of age and 8% to 33% in those 30 years of age or older. It can be concluded that between 10 to 25 percent of adolescents and adults are susceptible to pertussis and thus play a role in its transmission.
Antigenic components of *B. pertussis* believed to contribute to protective immunity include: pertussis toxin; filamentous hemagglutinin; and pertactin (69kDa). Although the role of these antigens in providing protective immunity in humans is not well understood, clinical trials which evaluated candidate acellular DTP vaccines manufactured by GlaxoSmithKline supported the efficacy of three component INFANRIX^{TM} (DTaP). Recently published data suggests a higher importance of the PT and pertactin (69kDa) components in providing protection against pertussis.

Poliomyelitis

Poliovirus is an enterovirus that belongs to the picornavirus family. Three serotypes of poliovirus have been identified (types 1, 2 and 3). Poliovirus is highly contagious with the predominant mode of transmission being person-to-person via the fecal-oral route. Infection may be spread indirectly through contact with infectious saliva or feces or by contaminated water or sewage.

Replication of poliovirus in the pharynx and intestine is followed by a viremic phase where involvement of the central nervous system can occur. While poliovirus infections are asymptomatic or cause nonspecific symptoms (low-grade fever, malaise, anorexia and sore throat) in 90% to 95% of individuals, 1% to 2% of infected persons will develop paralytic disease.

Following the introduction of inactivated poliovirus vaccines (IPV/ POLIO) in Canada in 1955, the indigenous disease has been eliminated. Since 1980, 12 paralytic cases have been reported in Canada, 11 of which were determined to be vaccine-associated paralytic poliomyelitis (VAPP), with Oral Polio Vaccine (OPV). The last reported case of VAPP occurred in 1995.

Forty seven studies involving over 19,000 infants and children have been conducted in developed and developing countries with GlaxoSmithKline's enhanced inactivated poliovirus vaccine, as trivalent IPV vaccine or as a part of DTPa-IPV based combinations.

Protective efficacy of pertussis

There is currently no correlate of protection defined for pertussis; however, the protective efficacy of GlaxoSmithKline DTPa (INFANRIX^{TM}) 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^{TM} 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.

As infants cannot begin their pertussis vaccination course until they are at least 6 weeks old and three doses of vaccine need to be given, vaccination does not confer complete protection until infants have received all 3 doses. Several studies have shown that adults are a significant source of pertussis in the first week of life. It could be expected that immunization 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 immunization. Booster immunization with BOOSTRIX®-POLIO, an acellular pertussis vaccine with reduced antigen content of diphtheria toxoids and pertussis, has demonstrated that the vaccine was immunogenic and well tolerated in clinical studies in which adolescents and adults have received BOOSTRIX®-POLIO.

STORAGE AND STABILITY

BOOSTRIX®-POLIO (combined diphtheria, tetanus, acellular pertussis (adsorbed) and inactivated poliomyelitis) vaccine must be stored at +2°C to +8°C. Do not use beyond the expiry date printed on the label and packaging.

DO NOT FREEZE; discard if vaccine has been frozen.

DOSAGE FORMS, COMPOSITION AND PACKAGING

The vaccine is available in pre-filled syringes and in glass vials* (0.5 mL) in packages of 1 or 10.

** Not available in Canada.*

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance:

Proper name: Combined diphtheria, tetanus, acellular pertussis (adsorbed) and inactivated poliomyelitis vaccine

Product Characteristics:

BOOSTRIX®-POLIO (combined diphtheria, tetanus, acellular pertussis and inactivated poliomyetitis) vaccine contains diphtheria toxoid, tetanus toxoid, three purified pertussis antigens [pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (69 kDalton outer membrane protein)] adsorbed onto aluminum salts and inactivated polio virus types 1, 2 and 3.

CLINICAL TRIALS

A summary of the pivotal and follow-up trials of BOOSTRIX®-POLIO in vaccinees of different ages is presented in Table 2.

Table 2: Summary of studies (Total cohort)

Study ID	Trial Design, Study Duration	Study and control vaccines	Number of subjects enrolled	Gender %Male Median Age (range)
One month after vaccination with BOOSTRIX®-POLIO (see Table 3)				
dTpa-IPV-001	Partially blinded, randomized, phase III , controlled. Approx. 1 month	1 vaccination visit • dTpa (BOOSTRIX®) + IPV (IPV *Merieux*®) • dTpa-IPV (3 lots*)	136 823	51.0% 5.0 years (4-8)
dTpa-IPV-002	Open, randomized, multicenter, phase II, controlled. Approx. 1 month	1 vaccination visit • DTPa-IPV (*Infanrix*-IPV™) • dTpa (BOOSTRIX®) + IPV (*Imovax* Polio®) • dTpa-IPV	111 220 441	41.2% 11.0 years (10-14)
dTpa-IPV-003	Open, randomised, multicentre, phase III, controlled	1 vaccination visit • Td-IPV (*Revaxis*®) • dTpa (BOOSTRIX®) + IPV (*Poliorix*™) • dTpa-IPV	270 270 266	44.3% 39.0 years (15-93)
Persistence 5 years after vaccination of children with BOOSTRIX®-POLIO (see Table 4) and second booster dose with BOOSTRIX®-POLIO (see Table 5)				
dTpa-IPV-008	Open, non-randomised, multicentre, phase IV	1 vaccination visit • dTpa (BOOSTRIX®) + IPV (IPV *Merieux*®) • dTpa-IPV (3 lots*) All subjects received a dose of BOOSTRIX®-POLIO	64 351	51.6% 11.0 years (9-14)

Vaccination of subjects ≥ 40 years of age with BOOSTRIX®- POLIO				
dTpa-034	Double blind, randomised, multicentre, phase III	• 3 doses dTpa (BOOSTRIX®) at month 0, 1 and 6 • 1 dose dTpa-IPV at month 0 and 2 doses of Td (*Tedivax*) at month 1 and 6 • 3 doses of Td (*Tedivax*) at month 0, 1 and 6	155 152 153	41.3% 57.0 years (40-85)

* 3 consistency lots of dTpa-IPV

More than 1500 subjects received BOOSTRIX®-POLIO (combined diphtheria, tetanus, acellular pertussis and inactivated poliomyetitis) vaccine in 3 pivotal clinical studies assessing seropositivity one month after receiving BOOSTRIX®-POLIO, children (4 to 8 years of age), adolescents (10 to 14 years of age) and adults (15 years of age and older). The children 4 to 8 years of age were previously vaccinated with four doses of DTPa or DTPa-based combinations and at least 3 doses of OPV or IPV. The adolescents 10 to 14 years of age had received primary and booster vaccination with DTPw in infancy and childhood and subjects in the 15 and older age range had in many cases received primary vaccination with diphtheria, tetanus, pertussis and polio vaccines. The percent seroprotective rates and vaccine responses of the 3 pivotal studies are presented in Table 3. Each of the 3 pivotal studies compared BOOSTRIX®-POLIO to BOOSTRIX® and IPV given separately.

Table 3: Percent seropositive* one month after vaccination with BOOSTRIX®-POLIO

Clinical Studies	Timing	Anti-D	Anti-T	Anti-PT	Anti-FHA	Anti-PRN	Anti-Polio		
							Type 1	Type 2	Type 3
4 to 8 years of age (n=779)	Pre	67.2	83.9	37.2	97.3	89.1	98.0	99.6	88.6
	Post	100.0	99.9	99.6	100.0	99.9	100.0	100.0	100.0
10 to 14 years of age (n=429)	Pre	73.7	95.8	53.5	98.8	78.8	96.9	97.6	79.4
	Post	100.0	100.0	99.3	100.0	100.0	100.0	100.0	100.0
≥ 15 years of age (n=261)	Pre	54.4	88.1	56.3	98.8	59.8	95.4	92.0	88.7
	Post	83.5	99.6	97.7	100.0	97.7	99.6	99.6	99.1

* Percentage of vaccinees having anti-diphtheria (Anti-D) and anti-tetanus (Anti-T) antibody titres > 0.1 IU/mL post vaccination (seroprotection) Percentage of vaccinees having anti-PT, anti-FHA, anti-PRN antibody titres ≥ 5 EL.U/mL; percentage of vacinees having anti-polio seroprotective antibody titres ≥ 8.
Pre = blood sample taken just prior to booster vaccination
Post = blood sample taken approximately 1 month after booster dose.

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

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

A total of 344 children vaccinated with BOOSTRIX®-POLIO between 4 and 8 years of age had antibody persistence five years later (see Table 4):

Table 4 Persistence of Responses Observed 5 Years after Vaccination with BOOSTRIX®-POLIO

Antigen	Response[1]	Number of Subjects (N)	Children from the age of 4 -8 years % vaccinees demonstrating response (CI)
			5 years persistence[3]
Diphtheria	≥ 0.1 IU/ml	341	89.4% (85.7-92.5)
	≥ 0.016 IU/ml[2]		98.2% (96.3-99.2)
Tetanus	≥ 0.1 IU/ml	342	98.5% (96.6-99.5)
Pertussis			
Pertussis toxoid	≥ 5 EL.U/mL	337	40.9% (35.7-46.4)
Filamentous haemagglutinin	≥ 5 EL.U/mL	340	99.7% (98.4-100)
Pertactin	≥ 5 EL.U/mL	342	97.1% (94.7-98.6)
Poliovirus			
Poliovirus type 1	≥ 8 ED50	340	98.8 % (97.0-99.7)
Poliovirus type 2	≥ 8 ED50	341	99.7% (98.4-100)
Poliovirus type 3	≥ 8 ED50	341	97.1% (94.7-98.6)

[1] 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.
[2] 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).
[3] Children were 9-13 years old at the time of persistence measurement
N = number of subjects with available results
CI = Confidence Interval (95%)

The immunogenicity of BOOSTRIX®-POLIO, administered 5 years after a previous booster dose of BOOSTRIX®-POLIO 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 (see Table 5).

Table 5 Immunogenicity of a second booster dose of BOOSTRIX®-POLIO administered 5 years after the first dose in children 4 to 8 years of age

Antigen	Response[1]	Number of subjects (N)	Children 9 to 13 years % vaccinees demonstrating response (CI)
Diphtheria	≥ 0.1 IU/mL	336	100% (98.9-100)
Tetanus	≥ 0.1 IU/mL	336	100% (98.9-100)
Pertussis			
Pertussis toxoid	≥ 5 EL.U/mL	335	99.7% (98.3-100)
Filamentous haemagglutinin	≥ 5 EL.U/mL	336	100% (98.9-100)
Pertactin	≥ 5 EL.U/mL	336	100% (98.9-100)
Poliovirus			
Poliovirus type 1	≥ 8 ED50	335	100% (98.9-100)
Poliovirus type 2	≥ 8 ED50	335	100% (98.9-100)
Poliovirus type 3	≥ 8 ED50	333	100% (98.9-100)

(1) Response: Where, one month after the second booster dose, 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.
N = number of subjects with available results
CI = Confidence Interval (95%)

After administration of one dose of BOOSTRIX®-POLIO to 140 adults ≥ 40 years of age that had not received any diphtheria and tetanus containing vaccine in the past 20 years, at least 96.4% of adults were seropositive for all three pertussis antigens and 77.7% and 95.7% were seroprotected against diphtheria and tetanus, respectively. After administration of two additional doses of a diphtheria and tetanus containing vaccine one and six months after the first dose of BOOSTRIX®-POLIO, the seroprotection rates for diphtheria and tetanus reached 100%.

Diphtheria and Tetanus
One month after vaccination, 100% of subjects up to 14 years of age and 83.5% of the subjects 15 years of age and older were seroprotected against diphtheria (≥0.1 IU/mL). One month after vaccination all subjects up to 14 years of age and 99.6 % of the subjects 15 years of age and older had seroprotective anti-tetanus antibody concentrations (≥0.1 IU/mL).

Polio
More than 99% of subjects were seropositive to all three polio types one month after a booster dose of BOOSTRIX®-POLIO.

Pertussis
One month after vaccination, over 97.7% of subjects who received BOOSTRIX®-POLIO were seropositive for anti-PT, anti-FHA or anti-PRN antibodies (≥5 EL.U/mL).

The pertussis antigens contained in BOOSTRIX®-POLIO are an integral part of the paediatric acellular pertussis combination vaccine (Infanrix™), for which efficacy after primary vaccination has been demonstrated in a household contact efficacy study. The antibody titres to all three pertussis components following vaccination with BOOSTRIX®-POLIO were at least as high or higher than those observed during the household contact efficacy trial. Based on these comparisons, BOOSTRIX®-POLIO would provide protection against pertussis, however the degree and duration of protection afforded by the vaccine are undetermined.

DETAILED PHARMACOLOGY

Not applicable.

MICROBIOLOGY

Not applicable.

TOXICOLOGY

Intramuscular administration during the organogenesis phase of pregnancy of 100 µl BOOSTRIX® (dTpa) to rats previously primed with INFANRIX™ (DTaP) vaccine or 100 µl dTpa-IPV vaccine to rats previously primed with INFANRIX™ -IPV (DTPa-IPV) was well tolerated during pregnancy and lactation and both treatment regimes were considered to be a no-toxic-effect-level for the parental female.

The treatment regime outlined for BOOSTRIX® (dTpa) vaccine was considered to be a no-observed-effect-level (NOEL) for pre- and post-natal survival and development of the offspring. Although an isolated and slight retardation of some ossification parameters was observed among dTpa-IPV treated fetuses on Day 20 gestation, no sustained effects were observed after parturition. Post-natal survival and development measures in the offspring were unaffected and therefore, this treatment regime was designated a no-observed-adverse-effect-level (NOAEL).

There were no biologically significant effects of treatment on bodyweight or bodyweight change either before pairing or throughout gestation or lactation.

Bodyweight change, relative to Day 0 of gestation was significantly lower than Control for Group 3 (dTpa-IPV) from Day 6-17 of gestation. However, bodyweight gains from Day 6 of gestation (the first day of dosing during gestation) were similar to Control and intergroup differences were considered to be of no toxicological significance.

The clinical significance of these observations is unknown.

Nonclinical data obtained with BOOSTRIX®-POLIO reveal no specific hazard for humans based on conventional studies of female fertility and embryo-fetal development in rats and rabbits, and also parturition and postnatal toxicity in rats (up to the end of the lactation period).

REFERENCES

1. Biological products; bacterial vaccines and toxoids; implementation of efficacy review. Federal Register. Friday, December 13, 1985; Vol. 50 (No. 240):51002-51117.

2. Campins-Marti M, Cheng HK, Forsyth K., Guiso N, Halperin S, Huang LM et al. Recommendations are needed for adolescent and adult pertussis immunisation: rationale and strategies for consideration. Vaccine 2001; 20 641-646.

3. Canada Communicable Disease Report, Volume 26, May 1, 2000.

4. Centers for Disease Control. General Recommendations on Immunization Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP). MMWR. 2002; Vol. 51 (RR-02):1-36.

5. Centers for Disease Control. Diphtheria, tetanus, and pertussis: Recommendations for vaccine use and other preventive measures. Recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR. 1991;Vol.40 (RR-10):1-28.

6. Centers for Disease Control and Prevention. Poliomyelitis Prevention in the United States: Introduction of a sequential vaccination schedule of inactivated poliovirus vaccine followed by oral poliovirus vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1997;46 (No.RR-3):1-25.

7. Centers for Disease Control and Prevention. Tetanus Surveillance—United States, 1995-1997. MMWR.1998;Vol.47(No. SS-2):1-13.

8. Centers for Disease Control and Prevention. Use of vaccines and immune globulins for persons with altered immunocompetence. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 1993;Vol. 42 (RR-4):1-3.

9. Cherry JD, Gornbein J, Heininger U, Stehr K. A search for serologic correlates of immunity to Bordetella pertussis cough illness. Vaccine 1998; 20: 1901-6.

10. Cowell JL, et al. Prospective protective antigens and animal models for pertussis. In: Leive L and Schlessinger D, eds. Microbiology-1984. Washington, DC: American Society for Microbiology, 1984, pp. 172-175.

11. Edwards K. Pertussis in older children and adults. Adv Paedr Infect Dis 1997; 13: 49-77.

12. Faden HS. Pilioviruses. Ped Infect Dis. 1977;249:1282-1287.

13. Greco D, Salmeso S, Mastrantonio P, Guiliano M, Tozzi AE, Anemona A, et al. A controlled trial of two acellular vaccines and one whole-cell vaccine against pertussis. N Engl J Med. 1996;334(6):341-348.

14. Gustafsson L, Hallander HO, Olin P, Reizenstein E, Storsaeter J. A controlled trial of a two-component acellular, a five-component acellular, and a whole-cell pertussis vaccine. N Engl J Med. 1996;334(6):349-355.

15. Kendrick PL. Secondary familial attack rates from pertussis in vaccinated and unvaccinated children. Am J Hygiene. 1940;32:89-91.

16. National Advisory Committee on Immunization: Canadian Immunization Guide, Seventh Edition. Minister of Public Works and Government Services Canada, 2006.

17. Nennig ME, Shinefield HR, Edwards KM, Black SB, Fireman BH. Prevalence and incidence of adult pertussis in an urban population. JAMA. 1996;Vol. 275 (21):1672-1674.

18. Schmitt H-J, von Konig CH, Neiss A, Bogaerts H, Bock HL, Schult-Wissermann H. Efficacy of acellular pertussis vaccine in early childhood after household exposure. JAMA. 1996;275(1):37-41.

19. Shahin RD, Brennan MJ, Li ZM, Meade BD, Manclark CR. Characterization of the protective capacity and immunogenicity of the 69-kD outer membrane protein of Bordetella pertussis. J Exp Med. 1990;171(1):63-73.

20. Storsaeter J, Hallander HO, Gustafsson L, Olin P. Levels of anti-pertussis antibodies related to protection after household exposure to Bordetella pertussis. Vaccine 1998; 20: 1907-16.

21. The role of the acellular pertussis vaccine and the demise of 'Pertussis Pete' Canadian Journal of Infectious Diseases, January/ February 2001.

22. Tran Minh NN, Hi Q, Ramalho A, Kaufhold A, Viljanen MK, Arvilommi H, Mertsola J. Acellular vaccines containing reduced quantities of pertussis antigens as a booster in adolescents. Pediatrics; 1999; 104(6):1377-1378.

23. Turnbull FM, Heath TC, Jalaludin BB, Burgess MA, Ramalho AC. A randomized trial of two acellular pertussis vaccines (DTPa and Pa) and a licensed diphtheria-tetanus vaccine (Td) in adults Vaccine; 2000 19(6):628-636.

24. Van der Wielen M, Van Damme P, Joossens E, Francois G, Meurice F, Ramalho A. A randomized controlled trial with diphtheria-tetanus-acellular pertussis (DTPa) vaccine in adults. Vaccine; 2000;18(20):2075-2082.

PART III: CONSUMER INFORMATION

BOOSTRIX®-POLIO
Combined diphtheria, tetanus, acellular pertussis (adsorbed) and inactivated poliomyelitis vaccine

This leaflet is part III of a three-part "Product Monograph" published when BOOSTRIX®-POLIO vaccine was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about BOOSTRIX®-POLIO. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
BOOSTRIX®-POLIO is a vaccine used in adults and children 4 years of age and above for protection against diphtheria, tetanus (lockjaw) and pertussis (whooping cough) and poliomyelitis (polio).

Vaccination is the best way to protect against these diseases.

What it does:
The vaccine works by causing the body to produce its own protection (antibodies) against these diseases.

When it should not be used:
Do not use BOOSTRIX®-POLIO if:

- you or your child has previously had any allergic reaction to BOOSTRIX®-POLIO, or any ingredient contained in this vaccine. The active substances and other ingredients in BOOSTRIX®-POLIO are listed below. Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue.
- you or your child has previously had an allergic reaction to any vaccine against diphtheria, tetanus, pertussis (whooping cough) or poliomyelitis diseases.
- you or your child experienced problems of the nervous system (encephalopathy) within 7 days after previous vaccination with a vaccine against pertussis disease.
- you or your child experienced problems with the brain or nerves after previous vaccination with a vaccine against diphtheria and/or tetanus.
- you or your child has a severe infection with a high temperature (over 40°C). A minor infection such as a cold should not be a problem, but talk to your doctor first.
- you are pregnant.

What the medicinal ingredient is:
The active substances contained in BOOSTRIX®-POLIO are: combined diphtheria and tetanus toxoids, three purified pertussis toxoids, [pertussis toxoid, filamentous haemagglutinin and pertactin (69 kiloDalton outer membrane protein)] and inactivated poliovirus.

None of the components in the vaccine are infectious.

What the important nonmedicinal ingredients are:
Medium 199 (as stabilizer containing amino acids, mineral salts, vitamin and other substances), sodium chloride, water for injection. Formaldehyde, neomycin and polymycin are present as traces.

What dosage forms it comes in:
BOOSTRIX®-POLIO is presented as a cloudy white sterile suspension in pre-filled syringes and glass vials in packages of 1 or 10. Upon storage, a white solid may be seen. This is normal.

WARNINGS AND PRECAUTIONS

BEFORE you use BOOSTRIX®-POLIO talk to your doctor or pharmacist if:

- you or your child have a family history of convulsions.
- your child is suffering from neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy (disease of brain).
- you or your child has a bleeding problem or bruises easily. BOOSTRIX®-POLIO should be given with caution since bleeding may occur following vaccination.
- you or your child had any problems (such as a high fever, collapse or shock-like state or persistent crying lasting 3 hours or more) within 48 hours or fits (with or without fever) within 3 days of vaccination with a vaccine against pertussis.
- you or your child has a high temperature (over 38°C)
- you or your child has any known allergies.
- you or your child is taking any other medicine or has recently received any other vaccine.
- you or your child has any serious health problem.
- your child is younger than 4 years of age.
- you are pregnant or breastfeeding.

Fainting can occur following, or even before, any needle injection; therefore, tell the doctor or nurse if you or your child fainted with a previous injection.

INTERACTIONS WITH THIS MEDICATION

Patients receiving immunosuppressive therapy or patients with immunodeficiency may not be fully protected against disease after receiving BOOSTRIX®-POLIO.

PROPER USE OF THIS MEDICATION

Usual dose:
The dose of BOOSTRIX®-POLIO (combined diphtheria, tetanus, acellular pertussis (adsorbed) and inactivated poliomyelitis vaccine) is 0.5 mL.

The doctor will give BOOSTRIX®-POLIO as an injection into the muscle.

The vaccine should never be given into a vein.

Missed Dose:
If you or your child misses a scheduled injection, talk to your doctor and arrange another visit.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all vaccines, BOOSTRIX®-POLIO may occasionally cause unwanted effects.

As with other vaccines, you or your child may feel pain at the injection site, or you may see some redness and swelling at this site. However, these reactions usually clear up within a few days.

In children 4 to 9 year of age, very common side effects (in more than 1 in 10 doses of the vaccine) after having BOOSTRIX®-POLIO are local pain, redness and swelling and sleepiness. Common side effects (in more than 1 in 100 doses of the vaccine) after having BOOSTRIX®-POLIO are injection site reactions (such as bleeding), headache, fever, loss of appetite and irritability.

Uncommon side effects (in more than 1 in 1,000 doses of the vaccine) after having BOOSTRIX®-POLIO, swollen glands, problems sleeping, lack of interest, dry throat, gastro-intestinal symptoms (such as stomach pain, , nausea, vomiting and diarrhea) and fatigue.

In adults, adolescents and children from the age of 10 years onwards, very common side effects (in more than 1 in 10 doses of the vaccine) after having BOOSTRIX®-POLIO are local pain, redness and swelling, fatigue and headache.

Common side effects (in more than 1 in 100 doses of the vaccine) after having BOOSTRIX®-POLIO are injection site reactions (such as bruising) and fever more than 38°C.

Uncommon side effects (in more than 1 in 1,000 doses of the vaccine) after having BOOSTRIX®-POLIO are oral herpes, tingling or numbness of the hands and feet, loss of appetite, swollen glands, sleepiness, dizziness, asthma, itching, joint and muscle pain, fever more than 39°C, chills and pain.

If these events continue or become severe, tell your doctor.

As with other vaccines in any age group, allergic reactions may occur very rarely (in less than 1 in 10,000 of doses of the vaccine). These may be local or widespread rashes that may be itchy or blistering, swelling of the eyes, mouth, tongue or throat, difficulty in breathing or swallowing, fits (with or without fever), hives, a hard lump at the injection site, large swelling of the vaccinated limb, unusual weakness, a sudden drop in blood pressure and loss of consciousness. Such reactions may occur before leaving the doctor's office. However, you should seek immediate treatment in any event.

If you or your child develops any other symptom within days following the vaccination, tell your doctor as soon as possible.

Do not be alarmed by this list of possible side effects. It is possible that you or your child will have no side effects from vaccination.

This is not a complete list of side effects. For any unexpected effects while taking BOOSTRIX®-POLIO, contact your doctor or pharmacist.

HOW TO STORE IT

Store BOOSTRIX®-POLIO in a refrigerator at 2°C to 8°C.

Store in the original package in order to protect from light.
Do not freeze. Freezing destroys the vaccine.

Keep out of the reach and sight of children.

Do not use after the expiry date which is stated on the carton. The date for last use corresponds to the last day of that month mentioned.

REPORTING SUSPECTED SIDE EFFECTS

To monitor vaccine safety, the Public Health Agency of Canada collects case reports on adverse events following immunization.

For health care professionals:
If a patient experiences an adverse event following immunization, please complete the appropriate Adverse Events following Immunization (AEFI) Form and send it to your local Health Unit in your province/territory.

For the General Public:
Should you experience an adverse event following immunization, please ask your doctor, nurse, or pharmacist to complete the Adverse Events following Immunization (AEFI) Form.

If you have any questions or have difficulties contacting your local health unit, please contact Vaccine Safety Section at Public Health Agency of Canada:

By toll-free telephone: 1-866-844-0018
By toll-free fax: 1-866-844-5931
By email: caefi@phac-aspc.gc.ca
At the following website:
http://www.phac-aspc.gc.ca/im/vs-sv/index-eng.php

By regular mail:
The Public Health Agency of Canada
Vaccine Safety Section
130 Colonnade Road
Ottawa, Ontario
K1A 0K9 Address Locator 6502A

NOTE: Should you require information related to the management of the side effect, please contact your health care provider before notifying the Public Health Agency of Canada. The Public Health Agency of Canada does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:
http://www.gsk.ca
or by contacting the sponsor, GlaxoSmithKline Inc.
7333 Mississauga Road
Mississauga, Ontario L5N 6L4
1-800-387-7374

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