

Boostrix Polio

**Diphtheria, tetanus, pertussis (acellular, component) and poliomyelitis
(inactivated) vaccine (adsorbed, reduced antigen(s) content)
Suspension for injection**

QUALITATIVE AND QUANTITATIVE COMPOSITION

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)
<i>Bordetella pertussis</i> 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) and aluminium phosphate (AlPO ₄)	0.3 milligrams Al ³⁺ 0.2 milligrams Al ³⁺
² propagated in VERO cells	

Boostrix Polio is a turbid white suspension. Upon storage, a white deposit and clear supernatant can be observed. This is a normal finding.

CLINICAL INFORMATION

Indications

Boostrix Polio is indicated for booster vaccination against diphtheria, tetanus, pertussis and poliomyelitis of individuals from the age of three years onwards.

Dosage and Administration

Posology

A single 0.5 ml dose of the vaccine is recommended.

Boostrix Polio may be administered from the age of three years onwards. Boostrix Polio should be administered in accordance with official recommendations and/or local practice regarding the use of vaccines with reduced content of diphtheria toxoid plus tetanus toxoid in combination with pertussis and poliomyelitis antigens.

Boostrix Polio may be administered to adolescents and adults with unknown vaccination status or incomplete vaccination against diphtheria, tetanus and pertussis as part of an immunisation series against diphtheria, tetanus, pertussis and polio (see *Pharmacodynamics*). Based on data in adults, two additional doses of a diphtheria and tetanus containing vaccine are recommended one and six months after the first dose to maximize the vaccine response against diphtheria and tetanus.

Boostrix Polio can be used in the management of tetanus prone injuries in persons who have previously received a primary vaccination series of tetanus toxoid vaccine. Tetanus immunoglobulin should be administered concomitantly in accordance with official recommendations.

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

Method of administration

Boostrix Polio is for deep intramuscular injection, preferably in the deltoid region (see also *Warnings and Precautions*).

Contraindications

Boostrix Polio should not be administered to subjects with known hypersensitivity to any component of the vaccine (see *Quantitative and Qualitative composition* and *List of Excipients*) or to subjects having shown signs of hypersensitivity after previous administration of diphtheria, tetanus, pertussis or poliomyelitis vaccines.

Boostrix Polio 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, tetanus and poliomyelitis vaccines.

Boostrix Polio 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 *Warnings and Precautions*).

Warnings and Precautions

It is good clinical practice that vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination 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.

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

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

- Temperature of $\geq 40.0^{\circ}\text{C}$ (rectal) 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.

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. According to available clinical data, the risk of such reactions is lower with acellular pertussis vaccines than with whole cell pertussis vaccines.

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 Polio should in no circumstances be administered intravascularly.

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 two minutes.

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.

A history of febrile convulsions, a family history of convulsions, a family history of Sudden Infant Death Syndrome (SIDS) and a family history of an adverse event following DTP vaccination do not constitute contraindications.

Human Immunodeficiency Virus (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.

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.

Interactions

Boostrix Polio can be given concomitantly with any of the following monovalent or combination vaccines: measles, mumps, rubella, varicella and human papilloma virus vaccine (see *Adverse Reactions*).

The sequential administration of combined dTpa-IPV followed by Cervarix one month later tended to elicit lower anti-HPV-16 and anti-HPV-18 GMTs compared to Cervarix alone. The clinical relevance of this observation is not known.

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

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

As with other vaccines, it may be expected that in patients receiving immunosuppressive therapy or patients with immunodeficiency an adequate immunologic response may not be achieved.

Pregnancy and Lactation

Fertility

No human data available. Animal studies do not indicate direct or indirect harmful effects with respect to female fertility.

Pregnancy

The use of Boostrix Polio may be considered during the third trimester of pregnancy.

For data relating to the prevention of pertussis disease in infants born to women vaccinated during pregnancy, see section *Pharmacodynamics*.

Safety data from a prospective observational study where Boostrix (dTpa component of Boostrix Polio) was administered to pregnant women during the third trimester (793 pregnancy outcomes) as well as data from post-marketing surveillance where pregnant women were exposed to Boostrix Polio or to Boostrix have shown no vaccine related adverse effect on pregnancy or on the health of the foetus/newborn child.

As with other inactivated vaccines, it is not expected that the polio antigens contained in Boostrix Polio would harm the foetus.

Human data from prospective clinical studies on the use of Boostrix Polio during the first and second trimester of pregnancy are not available.

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.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or post-natal development.

Boostrix Polio should only be used during pregnancy when the possible advantages outweigh the possible risks for the foetus.

Lactation

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

It is unknown whether Boostrix Polio is excreted in human breast milk.

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

Effects on Ability to Drive and Use Machines

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

Adverse Reactions

Clinical Trial Data

The safety profile presented in Table 1 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 local injection site reactions (pain, redness and swelling) reported by 31.3 – 82.3% of subjects overall. These had their onset within the first day after vaccination. All resolved without sequelae.

Adverse reactions reported are listed according to the following frequency:

Very common	≥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

Table 1: Adverse reactions reported in clinical trials with Boostrix Polio

<i>System Organ Class</i>	<i>Frequency</i>	<i>Adverse reactions</i>	
		<i>Children from 4 to 9 years of age</i>	<i>Adults, adolescents and children from the age of 10 years onwards</i>
<i>Infections and infestations</i>	Uncommon		oral herpes
<i>Blood and lymphatic system disorders</i>	Uncommon	lymphadenopathy	lymphadenopathy
<i>Metabolism and nutrition disorders</i>	Common	anorexia	
	Uncommon		decreased appetite
<i>Psychiatric disorders</i>	Common	irritability	
	Uncommon	sleep disorder, apathy	
<i>Nervous system disorders</i>	Very common	somnolence	headache
	Common	headache	
	Uncommon		paraesthesia, somnolence, dizziness
<i>Respiratory, thoracic and mediastinal disorders</i>	Uncommon	dry throat	asthma
<i>Gastrointestinal disorders</i>	Common		gastrointestinal disorders
	Uncommon	diarrhoea, vomiting, abdominal pain, nausea	
<i>Skin and subcutaneous tissue disorders</i>	Uncommon		pruritus
<i>Musculoskeletal and connective tissue disorders</i>	Uncommon		myalgia, arthralgia

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

Coadministration with MMR/V vaccines in children aged 3-6 years

Boostrix Polio was coadministered with MMR/V vaccines in 2 clinical studies with 406 children aged 3-6 years. In these studies, upper respiratory tract infection and rash were commonly reported. Fever, irritability, fatigue, loss of appetite and gastrointestinal disorders (including diarrhoea and vomiting) were reported with a higher frequency (very common) when compared to Table 1 while all other adverse reactions occurred at the same or lower frequency.

Adverse reactions additionally reported during clinical studies with Boostrix (dTpa component of Boostrix Polio), administered to 839 children (from 4 to 9 years of age) and 1931 adults, adolescents and children (above 10 years of age), are listed in Table 2:

Table 2: Adverse reactions reported in clinical trials with Boostrix

System Organ Class	Frequency	Adverse reactions	
		Children from 4 to 9 years of age	Adults, adolescents and children from the age of 10 years onwards
Infections and infestations	Uncommon		upper respiratory tract infection, pharyngitis
Nervous system disorders	Uncommon	disturbances in attention	syncope
Eye disorders	Uncommon	conjunctivitis	
Respiratory, thoracic and mediastinal disorders	Uncommon		cough
Gastrointestinal disorders	Common		nausea
	Uncommon		diarrhoea, vomiting
Skin and subcutaneous tissue disorders	Uncommon		hyperhidrosis, rash
Musculoskeletal and connective tissue disorders	Uncommon		joint stiffness, musculoskeletal stiffness
General disorders and administration site conditions	Very common		malaise
	Common		injection site reactions (such as injection site

			mass and injection site abscess sterile)
	Uncommon	injection site reactions (such as induration), pain	influenza like illness

Reactogenicity after repeat dose of Boostrix Polio or Boostrix

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 aged 15 years onwards without recent vaccination for diphtheria, tetanus, pertussis and polio, who received a dose of Boostrix Polio or another reduced-antigen content vaccine, followed by an additional dose of Boostrix Polio 10 years after, showed no increased reactogenicity.

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 Marketing Data

Table 3: Adverse reactions reported with Boostrix Polio during post-marketing surveillance

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

Overdose

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

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

Pharmaco-therapeutic group: Bacterial and viral vaccines combined, ATC code J07CA02

Immune response

The following immune responses were observed across studies one month post vaccination

with Boostrix Polio in children, adolescents and adults (Table 4).

Table 4: Immune response in children, adolescents and adults

Antigen	Response	Children aged 3 to 9 years N=1195 (% vaccinees)	Adults, adolescents and children aged from 10 years onwards N=923 (% vaccinees)
Diphtheria	≥ 0.1 IU/ml	100%	82.2 – 100%
Tetanus	≥ 0.1 IU/ml	99.9 – 100%	99.6 – 100%
Pertussis	Booster response*		
Pertussis toxoid		84.6 – 90.6%	79.8 – 94.0%
Filamentous haemagglutinin		90.1 – 98.8%	90.7 – 97.2%
Pertactin		94.2 – 96.6%	90.0 – 96.7%
Inactivated poliovirus	≥8 ED50		
type 1		98.8 – 100%	99.6 – 100%
type 2		99.2 – 100%	99.6 – 100%
type 3		99.4 – 100%	99.1 – 100%

N=number of subjects

*Booster response defined as:

- for initially seronegative subjects, antibody concentrations at least four times the cut-off (post-vaccination concentration ≥ 20 El.U/ml);
- for initially seropositive subjects with Pre booster vaccination concentration ≥ 5 El.U/ml and < 20 El.U/ml: an increase in antibody concentrations of at least four times the Pre booster vaccination concentration.
- for initially seropositive subjects with Pre booster vaccination concentration ≥ 20 El.U/ml: an increase in antibody concentrations of at least two times the Pre booster vaccination concentration

As with other adult-type Td 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.

Efficacy in protecting against pertussis

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 are 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.

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

Boostrix or Boostrix Polio 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 vaccination programme.

Details of each study design and results are provided in Table 5.

Table 5: VE against pertussis disease for infants below 3 months of age born to mothers vaccinated during the third trimester of pregnancy with Boostrix/Boostrix Polio

Study location	Vaccine	Study design	Vaccination Effectiveness
UK	Boostrix Polio	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, vaccine effectiveness in the infant may be lower than the figures in the table.

Persistence of the immune response

Five years following vaccination with Boostrix Polio, at least 89.4% of children from the age of 4 to 8 years were seroprotected or seropositive against all vaccine components, except for the pertussis toxoid component (40.9% of subjects were seropositive against pertussis toxoid).

Ten years following vaccination with Boostrix Polio, at least 78.7% of adults and adolescents were seroprotected or seropositive against all vaccine components.

Immune response after a repeat dose of Boostrix Polio

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.

In adults, one dose of Boostrix Polio administered 10 years after the previous dose, elicited a protective immune response in > 96.8% of the subjects (for the diphtheria antigen) and in 100% of the subjects (for the tetanus and polio antigens). The booster response against the pertussis antigens was between 74.2 and 98.4%.

Immune response in subjects without prior or with unknown vaccination history

In adolescents aged from 11 to 18 years, without previous pertussis vaccination and no vaccination against diphtheria and tetanus in the previous 5 years, one dose of Boostrix (dTpa component of Boostrix Polio) induced an antibody response against pertussis and all subjects were protected against tetanus and diphtheria.

In subjects \geq 40 years of age that had not received any diphtheria or tetanus containing vaccine in the past 20 years (including those who have never been vaccinated or whose vaccination status was unknown), one dose of Boostrix Polio induced an antibody response against pertussis and protected against tetanus and diphtheria in the majority of cases.

Pre-clinical Safety Data

Animal toxicology and/or pharmacology

Preclinical data reveal no special hazard for humans based on conventional studies of safety and of toxicity.

PHARMACEUTICAL PARTICULARS

List of Excipients

Medium 199 (as stabilizer), sodium chloride, water for injections.
Formaldehyde, polysorbate 80, neomycin sulphate, polymyxin B sulphate are present as residues from the manufacturing process.

Shelf Life

The expiry date is indicated on the label and packaging.

Special Precautions for Storage

Store in a refrigerator (2°C – 8°C).

Do not freeze. Discard if the vaccine has been frozen.

Protect from light.

The storage conditions are detailed on the packaging.

Nature and Contents of Container

Suspension for injection in pre-filled syringes (Type I glass) (0.5 ml) with rubber stoppers.

Not all presentations are available in every country.

Incompatibilities

Boostrix Polio should not be mixed with other vaccines in the same syringe.

Instructions for Use/Handling

Prior to use, the vaccine should be at room temperature and well shaken in order to obtain a homogeneous turbid white suspension. Prior to administration, the vaccine should be visually inspected for any foreign particulate matter and/or variation of physical aspect. In the event of either being observed, do not administer the vaccine.

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

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

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